Targeting Epigenetic Regulator Histone Deacetylase 6 in the Treatment of Cancer: A Computational Approach

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Certificate

This is to certify that the thesis entitled "**Targeting Epigenetic Regulator Histone Deacetylase 6 in the Treatment of Cancer: A Computational Approach**" by **Karthic K (212bm2359)** submitted to the National Institute of Technology, Rourkela for the Degree of Master of Technology is a record of bonafide research work, carried out by him in the Department of Biotechnology and Medical Engineering under my supervision and guidance.

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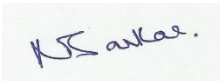

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Abstract

Targeting the, chromatin modifying enzyme, Histone deacetylase 6 has been a strategy that is recently identified to treat several cancers such as liver, lung and other tumours. Besides deacetylating histones, the enzyme also acts on proteins such as HSP90, Cortactin and α-tubulin that are involved in tumorigenesis. The present study combines the techniques of structure based and ligand based virtual screening methods to identify new drug compounds that could selectively inhibit HDAC6. The second catalytic domain of the enzyme was modelled and docking studies were performed on it with the compounds obtained from literature. The results of the docking were employed to screen the compounds for building a pharmacophore model. The Pharmacophore model was utilized in identifying 106 compounds from drugbank as hits. A genetic algorithm based QSAR model was developed to further screen the hits identified to 58 based on predicted activity. Free binding energy estimation was done for the 58 compounds and the poses with best binding energy and interactions are suggested as inhibitors of histone deacetylase 6.

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CHAPTER 1
INTRODUCTION

1.1.1. Introduction

1.1.2. Epigenetics

The term epigenetics relates to heritable changes in the gene expression without any actual change in the sequence of the DNA or in its expressed proteins.[1, 2] It takes control of expression and repression of the genes based upon the cues obtained from the environment. Some of the notable examples currently known are X- Chromosome inactivation in female mammalians, Identical twins diverging considerably as they age on, differential coat colours observed in female calico cats. It encompasses events such as DNA Methylation, Post translational modification to histone tails such as Acetylation, Methylation, Ubiquitination, Phosphorylation, Sumoylation etc. and small non coding RNA (miRNA, siRNA).[3]

Epigenetics plays a crucial role in the developmental process of a eukaryotic organism such as cellular differentiation and proliferation, it is also actively involved in the maintenance of several genes such as expression and silencing of Tumour suppression genes and oncogenes respectively. Any aberrations in the above episodes could lead to epigenetic diseases most importantly Cancer.

DNA Methylation

DNA Methylation is a process where methyl groups are added to Cytosine bases at CpG dinucleotide domains. Methylation of CpG dinucleotides generally leads to gene silencing, at the same time DNA hypermethylation at promoter regions may lead to repression of Tumour suppression genes (TSGs) which further promotes tumorigenesis. In Contrast reduced methylation of genes, hypomethylation affects the stablility of the genome by allowing certain lethal genes such as oncogenes to get expressed.[4, 5]

Post Translational Modifications at Histone Domains

146 base pairs of DNA is tightly wrapped around the octamer consisting four pairs of Histone subunits H2A, H2B, H3 AND H4.[6, 7] Each Histone domain is connected through a linker DNA. From the N-terminal region protrudes histone tail where a wide array of Post Translational Modifications (PTMs) occur. PTMs refers to covalent modification of histone tails by addition or removal of chemical groups such as acetyl, methyl etc at specific residues. PTMs play a crucial role in positioning of chromatin, which in turn affects the accessibility of genes to transcription factors.[8] Out of several PTMs, Histone acetylation/deacetylation and Histone methylation/ demethylation has been widely studied and best understood.

1.1.3. Histone Deacetylases (HDACs)

Histone Deacetylases (HDACs) are a family of enzymes that catalyse the removal of acetyl groups from the amino terminal of lysine residues of histone tails. This results in tighter wrapping of DNA around the histone octamer and blocking the access of DNA by Transcription Factors (TFs).[9] In contrast Histone acetyl transferases (HATs) produces an opposite effect by adding negatively charged acetyl groups to positively charged lysine residues.[10] This allows the DNA to free itself from the histone octamer and thereby binding of TFs. Essentially HDACs repress the gene expression whereas HATs facilitate gene expression.

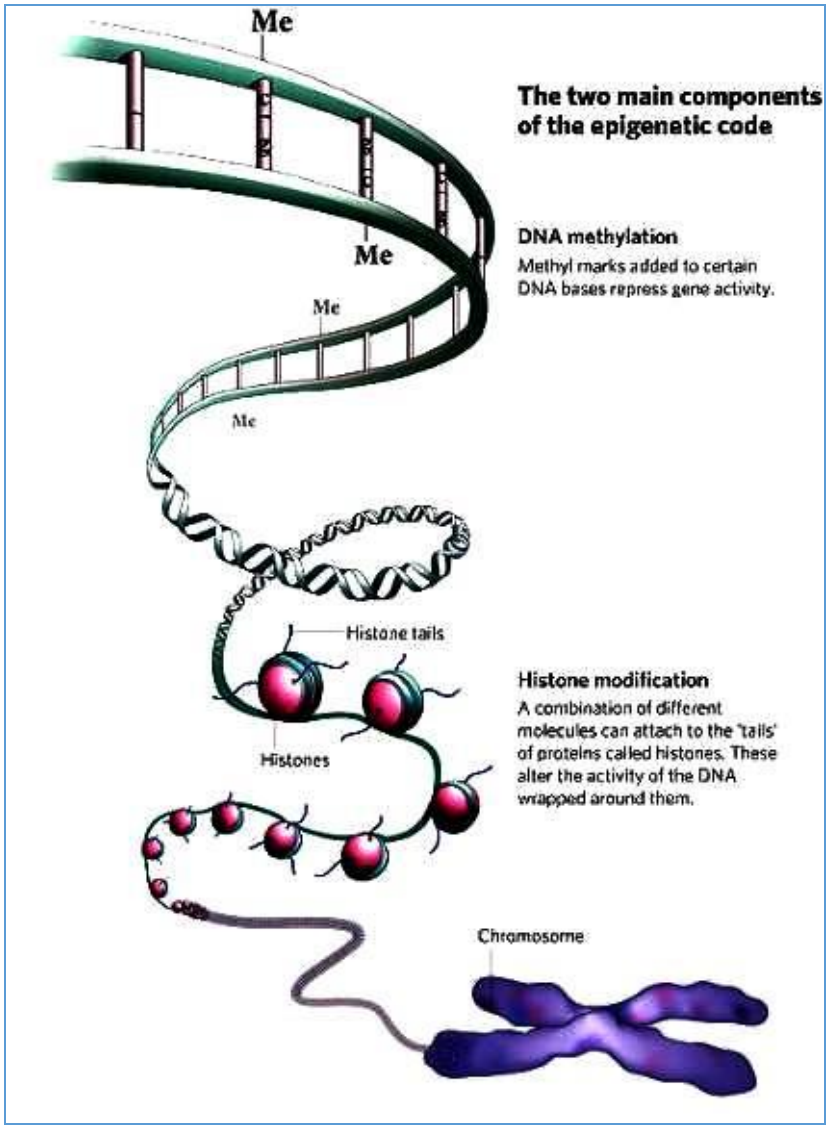


Figure 1. The two main components of epigenetics, DNA methylation and Histone modification.

Apart from its natural substrate Histone, HDACs target a wide range of proteins involved in regulatory functions such as cell cycle, cytoskeletal stability, cell proliferation, cell motility and apoptosis.[11, 12] Considering the fact that it plays a crucial role in the above functions, any aberrations could lead to serious conditions such as Cancer. HDACs has been the target of several inhibitors in the treatment of various cancers since overexpression of HDACs represses the expression of Tumour Suppressor Genes (TSGs).

18 different HDACs has been identified so far and are classified into four classes base upon their identity to yeast histone deacetylases.[9, 13] HDAC 1, 2, 3 and 8 are nuclear enzymes classified under Class I. Class II has two subclasses within, Class IIa and Class IIb containing HDAC 4, 7 and 9 and HDAC 6 and 10 respectively. Class II enzymes can shuttle between nucleus and cytoplasm. Class III also called Sirtuins are NAD+ dependent enzymes which includes Sirt 1 – 7. HDAC 11 the lone enzyme has been classified into Class IV. HDACs belonging to the Class I, II and IV are Zinc dependent proteins which is important for their catalytic activity.

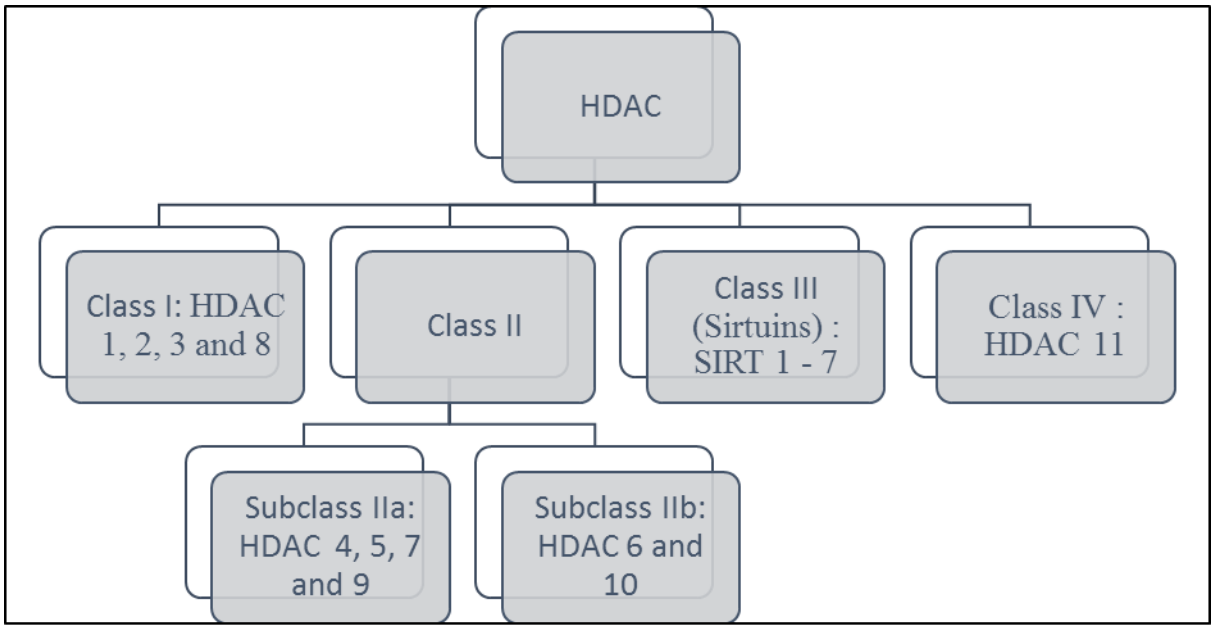


Figure 2. Classification of Histone Deacetylase (HDAC) family. Class I, II and IV are zinc dependent enzymes whereas Class III are NAD dependent enzymes.

1.1.4. Histone Deacetylase Inhibitors

As earlier mentioned HDACs are involved in the progression of variety of cancers such as breast cancer, colon cancer and several other solid tumours, there has been growing need to discover new inhibitors of HDACs.[14-16] Most of the inhibitors currently being targeted are small molecular compounds such as Hydroxamates, benzamides, carboxylates etc., At

present U.S Food and Drug Adminstration (FDA) has approved two drugs Vorinostat or SAHA and romidepsin in the treatment of Cutaneous T-Cell Lymphoma[17, 18]. Various other inhibitors are in the various stages of clinical trials. Despite with several potential inhibitors ready to be available, none of them are specific to any HDACs and all are categorised as pan inhibitors of HDACs. It has been found that pan inhibitors lead to several side effects such as nausea, anorexia, fatigue, anemia, cardiac arrhythemias and ECG changes when taken as a drug, which is understandable with the wide range of regulatory functions HDACs take part in.[16, 19]

The present study states the need to discover drugs specific to HDAC isoforms. HDAC6, a class IIb enzyme has been implicated in Oral Squamous cell cancer, Breast cancer, lung cancer, hepatocellular carcinoma etc., which are mostly due to anomalies related to deacetylase activity towards its key substrates such as α-tubulin, β-Catenin, HSP90 and Cortactin.[20-22]

1.1.5. Computer Aided Drug Discovery (CADD)

On an average, the US Pharmaceutical industry spends around US $60 billion in the search of new drugs for diseases such as Cancer, AIDS, Alzheimer's and Malaria. A new drug in order to hit the market, it will take around 10 – 15 years and US $500 – 800. It is a huge challenge in terms of time and money.[23, 24] A prospective drug may fail at any stage of clinical trials and may even be withdrawn after being approved if any concomitant reactions are observed. So it has been a norm for every pharmaceutical industry to reduce cost and save time with the help of computational power.

Since there are millions of compounds – synthetic and biological available in various databases, it is almost impossible to try out each compound experimentally for its ability in being a possible drug for a particular disease. Computational approach helps in screening out

most of the unlikely and unfeasible compounds during the vey initial stages of drug discovery. This approach has also been termed as Virtual Screening, it generally precedes the High throughput screening approach which is generally adopted. It basically optimizes the chances of lead identification with little expenditure and limited amount of time. Virtual Screening could be either Structure based or Ligand Based or sometimes both the approaches could be adopted together. Here again the input for any theoretical study like this is again data from experimental studies such as Protein Structure from crystallography or NMR , IC50 values from inhibiton studies etc.[25-27]

1.1.5.1. Structure Based Drug Discovery

It has been the typical and widely used approaches for potential lead identification and discovery. The data for this approach is protein structure obtained through X-Ray Crystallography, NMR or Homology Modelling Studies. Here a diverse set of small molecules are docked into the macromolecule by predicting the binding site of the protein. The docked protein-ligand complexes are analysed for their affinity and binding energy, best conformations and their hydrogen bonding ability. With those parameters the best docked pose will be identified and taken for further in-silico toxicity assays or for High Throughput Screening depending upon the number of screened compounds available in hand.

Molecular Docking

Docking is the most extensively used method in the rational drug design process to find out new compound that fits the profile of a drug for a particular disease. The preliminary requirement for a docking program is protein structure obtained from X-Ray Crystallography or NMR Spectroscopy or a Modelled protein using the sequence available in NCBI databases. The next step is predicting and analysing binding site of the protein using online servers available for this. The two basic components of any docking program are Search algorithm

and scoring function. The search algorithm predicts the best conformations for a compound to fit into the binding site and the Scoring function ranks the ligand conformations based upon their binding affinities.[28]

1.1.5.2. Ligand Based Drug Discovery

This approach is regarded as indirect one, where the structure of the target protein is not available and drug discovery is mainly carried out with the input of activity data available through experimental results. The methods that come under this approach are Pharmacophore modelling and Quantitative Structure Acitivity Relationship (QSAR).

Pharmacophore Modelling

According to IUPAC, a pharmcophore could be defined as "an ensemble of electronic and steric features that is necessary to ensure optimal supramolecular interactions with a specific biological target and to trigger its biological response "[29]. It searches for different conformations in a compound library and will try to match different pharmacophore features such as Hydrogen bond donor, Hydrogen bond acceptor, Negative Ionizable area, Positive Ionizable area, hydrophobic interactions, Aromatic Ring, Metal binding location. A model is built based upon the matched features between the compounds and the same model is latter used to screen large databases in search of similar compounds.[30]

Quantitative Structure Activity Relationship

QSAR is a statistical model which gives a mathematical equation that describes the relation between the structure, which is given in a mathematical form called descriptors and Biological or physic-chemical properties of the compound. The equation is later used to predict properties such as Biological Activity, Log P etc. QSAR models are also called

regression models which gives an R squared value based on the linearity of the compounds given to the model.[31, 32]

1.2. Objectives

i. To model the second catalytic domain of the enzyme Histone deacetylase6 with the Modeller.

ii. Minimizing the energy of the protein using Gromacs.

iii. Developing a Ligand – based pharmacophore model to search for compounds with similar pharmacophoric features in various database.

iv. To predict activity of the identified hits through a genetic algorithm based QSAR model.

v. Estimate the binding efficiency of the screened compounds and their interactions using Autodock Vina.

CHAPTER 2
LITERATURE REVIEW

2. Literature Review

2.1. Post Translational Modification at Histone Tails

Histone proteins are subjected to a wide array of post translational modifications which affects the chromatin position and there after transcription status of genes. Four pairs of histone proteins H2A, H2B, H3 and H4 forms an octamer and is wrapped around by DNA to form a nucleosome molecule. Out from the surface of histone protein protrudes a tail region which is the target of post translational machinery.[33-35] Histone tails comprise around 30% of the total individual mass of histone are found to protease sensitive.[36, 37] Methylation, Acetylation, Phosphorylation, Sumoylation, Ubiquitination and ADP ribosylation are PTMs that take place on histone tails.

2.2. Histone Deacetylases (HDACs)

Histone deacetylases (HDACs) also called Lysine Deacetylase (KDACs) mediates the regulation of gene expression by compacting the DNA around the hisone octamers. This is achieved by removal of acetyl groups from the ε-N- terminal of lysine residues on histone tails. Apart from histone they also deacetylase several other regulatory proteins which are involved in cell proliferation, cell differentiation, cytoskeletal stability and cell motility [38, 39]. In contrast Histone acetyl transferases (HATs) perform antagonistic functions by adding acetyl groups to the histone tails and allowing the DNA to free itself of histone octamers and make itself available for transcription [40, 41].

Around two decades before, Yoshida et al., has identified TSA induces differentiation and cell cycle arrest in cultured cells [42]. It was also found that TSA while inducing differentiation it actually inhibits HDAC, later Richon et al also observed hyperacetylated

proteins due to inhibition of HDACs [43]. In 2007, suberoylanilide hydroxamic acid (SAHA, vorinostat) was discovered as a drug to treat Cutaneaous T cell lymphoma while inhibiting all 11 classical HDACs. It was also found that the HDAC inhibitors have no toxic effects on normal cells but only on transformed cells [44]. Since then a large group of researchers have sought to discover new potential inhibitors of HDACs in the treatment of breast cancer, colon cancer, lung cancer and other tumours.

2.3. Histone Deacetylase 6

HDAC6 has been identified as cytoplasmic protein which apart from its natural substrate histone catalyses the deacetylation of α-tubulin which is associated with microtubulin network. The above process has direct influence on cytoskeletal stability and it the enzyme is also referred to as Tubulin Deacetylase due to its action [12, 13, 45]. In addition to α-tubulin, HDAC6 catalyses various cytoskeletal proteins such as HSP90, Cortactin, β-Catenin, Ku70 etc. [46-49]. HDAC6 is inhibited by Vorinostat and TSA, but lack of selectivity towards the enzyme particularly over HDAC1 prevents it being taken as potent inhibitors. Tubacin and Tubastatin A were found to have shown selectivity towards HDAC6, but due to their poor drug like properties deters it from proceeding to further clinical trials.[50, 51]

CHAPTER 3
METHODOLOGY

3. Methodology

3.1. Homology Modelling of HDAC6

Histone Deacetylase 6 (HDAC6) has been identified as cytosolic protein and it has sequence length of 1215 amino acid residues. HDAC6 was found to possess two catalytic domains CD1 and CD2 with residue positions from 73 - 455 and 479 – 845 respectively. It was also further identified that the Catalytic Domain 2 (CD2) is the main site for substrate deacetylation. Currently there is no crystal structure of HDAC6 with any of the catalytic domain is available. Homology modelling of CD2 of HDAC6 was performed with the template chosen as 3C0Y, crystal structure of HDAC7 which was available in the Protein Data Bank.

The Query sequence of HDAC6 was obtained from Uniprot and was later trimmed to include sequence of only CD2. Homology Modelling was done using Modeller 9.11, a freely available software.[52] It is a program which does comparative protein structure by satisfaction of spatial restraints. The query sequence was performed blast analyses to such for template structures in PDB with similar sequences. These template sequences were fed into Modeller along with the query sequence where it performed multiple sequence alignment and zeroed in on 3C0Y as template based upon the root mean square difference. Five models were generated using the chosen template, and the best model was selected by evaluating Dope score and GA341 score.

3.2. Validation of Homology Model

The model generated using Modeller was validated using Rampage [http://mordred.bioc.cam.ac.uk/~rapper/rampage.php] and Prosa[53], both online servers. Rampage assess the quality of protein structure by analysing it through Ramachandran plot. The protein structure in pdb format was given as input and it generates a plot with percentage

of residues present in favoured, allowed and outlier regions. On the other hand Prosa calculates Z-score and gives the output in the form of a plot with the Z-scores of all experimental derived structures. The quality of modelled protein is assessed by looking at the position while corresponding to experimental structures (X-Ray Crystallography and NMR).

3.3. Energy Minimization of Protein

The energy minimization of modelled protein was done using Gromacs 4.6.5, a molecular dynamics and simulation package in Linux environment.[54, 55] The topology file for the protein was prepared and a cubic box is generated with dimension of 0.7 d. The protein was put into the box and was solvated using water molecules. Gromos53a6 [56] forcefield was chosen and algorithm as Steepest descent to perform minimization.[57] 1000 steps was given for the steepest descent algorithm to converge the protein to its minimal energy state.

3.4. Virtual Screening of compounds targeting HDAC6

3.4.1. Molecular Docking

An exhaustive literature search has led to the identification of 819 compounds that showed varied inhibitory potential (Ranging from 0.002 – 68000 nM) against HDAC6.The residues that are involved in the active site were identified and the x,y and z coordinates of the active site residue was obtained. Autodock Vina, a freely available program was used to perform docking.[58] Compared to Autodock 4.2.1, Vina was reported to significantly increase the accuracy of the binding mode. The pdbqt files for the receptor and ligands were prepared using Autodock 4.2.1 in a batch manner. The pdbqt files and x, y and z coordinates of the receptor were fed to vina in a batch manner to perform docking for 819 compounds.

3.4.2. Ligand based pharmacophore modelling

Pharmacophore model generation was accomplished by Ligandscout 3.1.[59] The dataset for model generation was obtained by filtering out compounds from the docked results. Compounds having binding energy less than -7.0 and molecular weight less than or equal to 600 were discarded and the remaining 164 compounds were retained as dataset. Conformations for the compounds was generated by Omega, a component inbuilt in ligandscout with fast settings. The number of conformations to be generated was given as 25, RMS threshold was given as 0.8 and the rest of the settings being default.

3.4.2.1. Training Set and Test Set

For a successful pharmacophore model, preparation of training set with diverse features is crucial. 13 compounds having features such as Hydrogen bond acceptor, Hydrogen bond donor, Negative ionisable area and aromatic rings were assigned as training set and rest as test set.

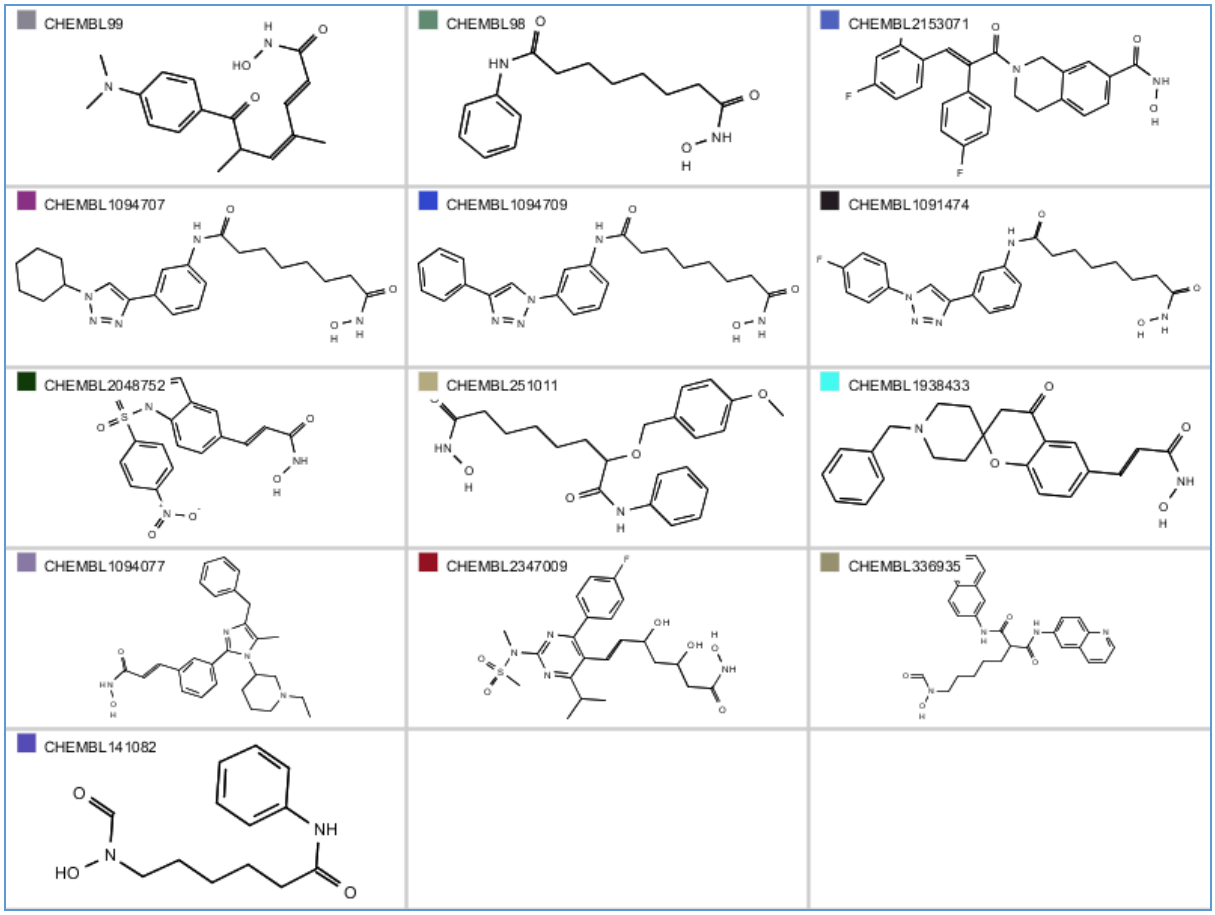


Figure 3. Training set molecules with features HBA, HBD, Hydrophobic and Negative ionisable areas used to develop pharmacophore model.

3.4.2.2. Model Generation

Pharmacophore model was generated with training set having 13 compounds. The scoring fuction was selected as Pharmacophore fit and atom overlap and Merged feature pharmacophore was chosen as Pharmoacophore type. The number of omitted features was given as 3 and exclusion volumes were allowed to be created. With other all settings being default, models were generated by mapping features of ligands to bring out a common pharmacophore.

3.4.2.3. Database Search for identification of hits

Creating and Loading database

Drugbank, a database for in-silico virtual screening contains 6381 compounds with more than 1500 being FDA approved. The compounds are freely available for downloading as Stucture data file (sdf). A database for Drugbank compounds was created in ligandscout from the structure data file. This database was further loaded into screening module of ligandscout for screening of compounds using the built pharmacophore.

Database Screening

The pharmacophore generated having top score was copied to screening perspective and performed screening to select molecules from Drugbank with similar pharmacophoric features. The Scoring function was selected as Pharmacophore-fit and screening mode was selected as match all query features. The maximum number of omitted features was given as zero and exclusion volumes was selected.

3.4.3. Quantitative Structure Activity Relationship

QSAR was performed to further screen the hits from drug bank identified through pharmacophore model. McQSAR, an open source software was employed for this.[60] McQSAR gives the output as a mathematical equation which is evolved over a sequence of generations using Genetic algorithm.

3.4.3.1. Model Generation

128 diverse set of compounds with activities ranging from 1 to 10000 nM were obtained from the literature and assigned as training set to develop QSAR model. The inputs for the program are descriptor file for the training set and an activity file corresponding to that. The descriptors for the training set was calculated using Padel Descriptor, a free java based tool. The parameter to be predicted by McQSAR is assigned as IC50 and the other settings such as

mutation probability and number of generations were given as 0.05 and 100 respectively. The rest other settings were default ones.

3.4.3.2. Prediction of activity

Out of several models generated, the model having best R^2 and Q^2 values (R^2 should be greater than 0.6 and Q^2 should be greater than 0.6). As the value of R^2 approaches 1, it indicates the linearity of model and its statistical predictability. The generated equation that describes the relation between the compounds and its activity was taken from the best model. The prediction run was carried by giving the equation file the compounds for which activity to be predicted as inputs. The activities for the hits obtained from Drugbank were predicted.

3.4.4. Estimation of Free Binding energy

Out of 106 Drugbank compounds for which activity has been predicted, 58 compounds were selected by screening compounds with Predicted IC50 in the range of 1 – 1000 nM. Docking was performed using Autodock Vina, the x, y and z active coordinates of the modelled protein was given and the compounds were docked in a batch process one by one. The binding energy and best conformations of docked Receptor – ligand complexes were obtained.

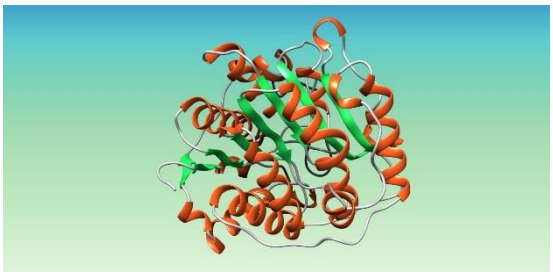
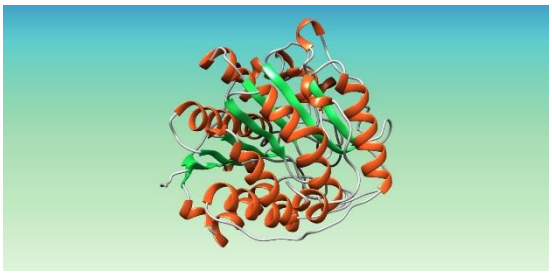
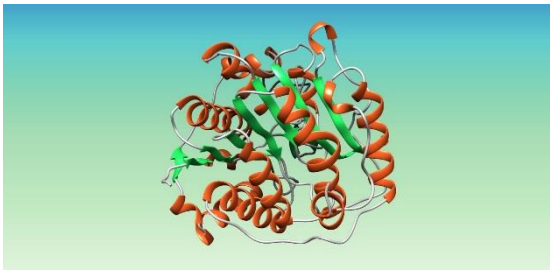
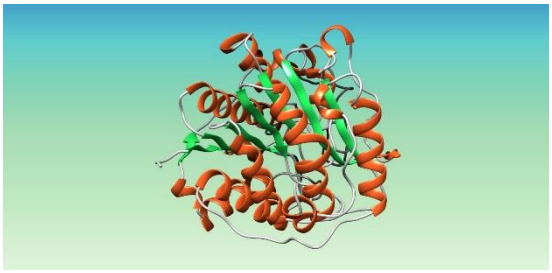
CHAPTER 4
RESULTS

4. Results

4.1. Homology Modelling

The BLAST search for structures with similar sequences has returned 7 proteins with more than 40 % identity. Out of those three structures, 2VQO, 4CBY and 3C0Y were further selected for modelling. A alignment file was generated between query sequence and template sequences. Later five models were generated by using the automodel class of modeller. The best model HDAC6.B99990002 was selected by evaluating the models with low DOPE potential score.

Model Generated	DOPE Score	Pictographic Representation

HDAC6.B99990001	-42404.44141	
HDAC6.B99990002	-42687.34766	
HDAC6.B99990003	-42327.76953	
HDAC6.B99990004	-41805.35156	

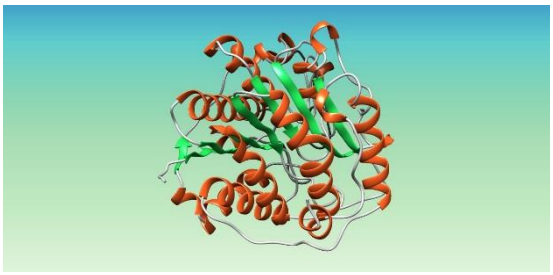
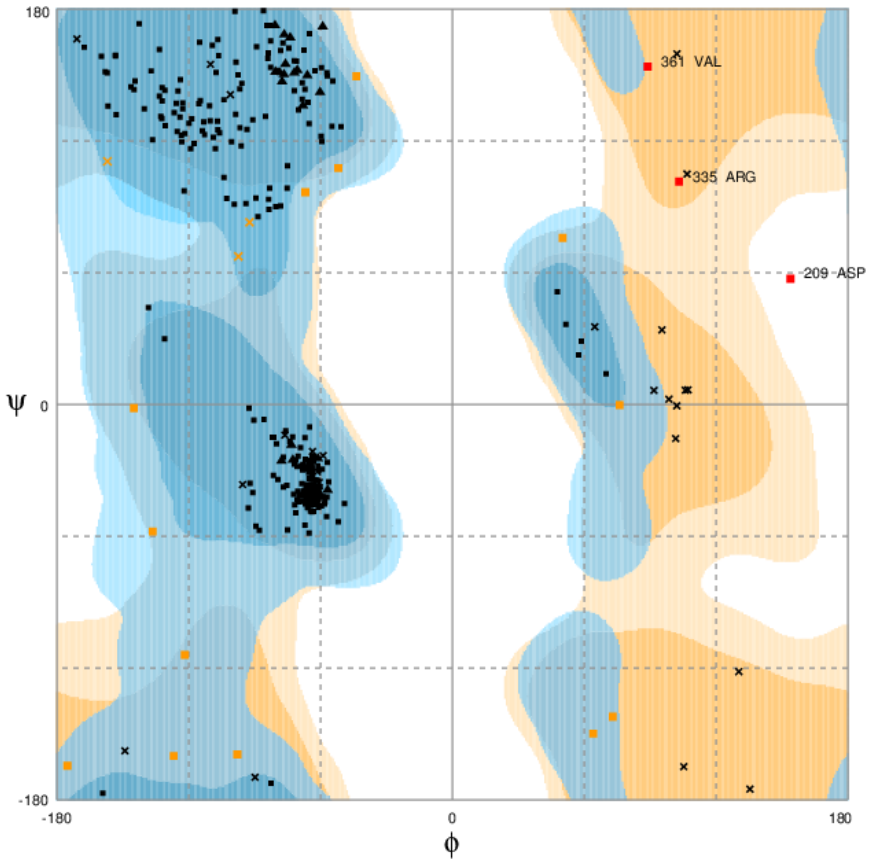
HDAC6.B99990005	-42229.28516	

Figure 4. Five models generated by Modeller with three proteins 2VQO, 4CBY and 3C0Y as template structures. The best model is the one with the lowest DOPE potential score.

4.1.1. Validation of Homology Model

The validation of the model HDAC6.B99990002 by Rampage has showed around 0.3% residues lying in the outlier region which is pretty common in the modelled proteins. The overall model quality was predicted by PROSA, which gave a Z-Score of -7.81 which is in agreement with X-Ray and NMR structures.

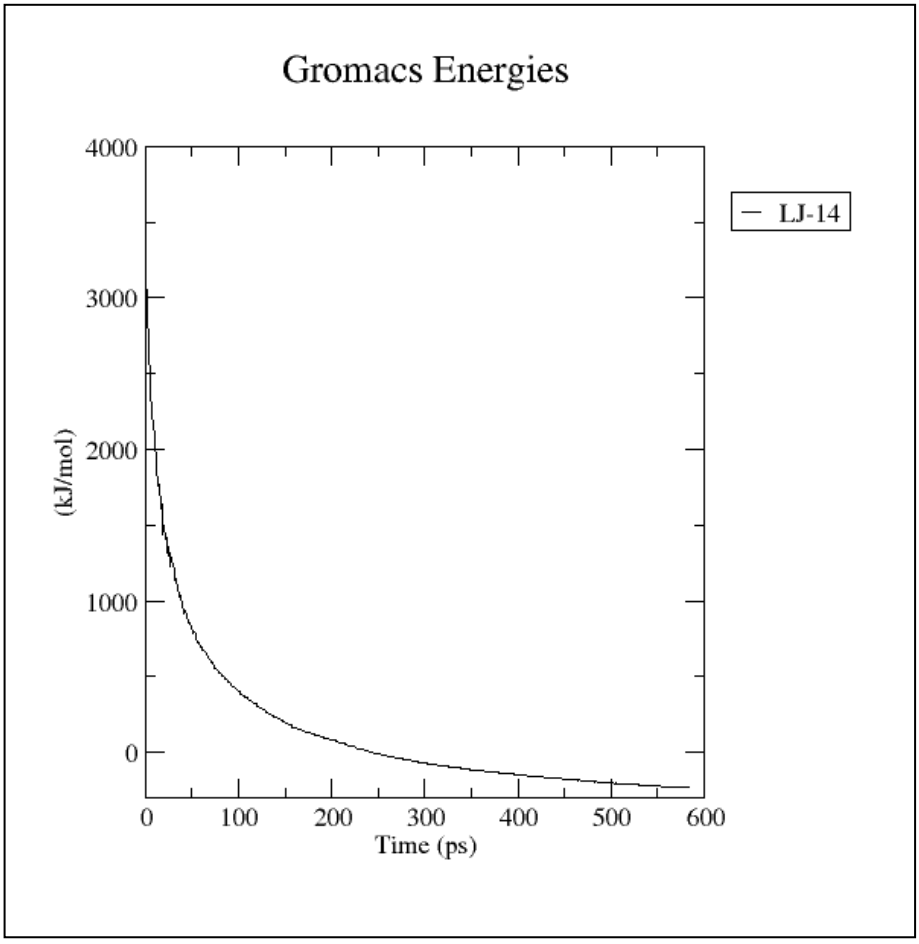


Number of residues in favoured region (~98.0% expected) : 354 (94.9%)
Number of residues in allowed region (~2.0% expected) : 16 (4.3%)
Number of residues in outlier region : 3 (0.8%)

RAMPAGE by Paul de Bakker and Simon Lovell available at http://www-cryst.bioc.cam.ac.uk/rampage/

Please cite: S.C. Lovell, I.W. Davis, W.B. Arendall III, P.I.W. de Bakker, J.M. Word, M.G. Prisant, J.S. Richardson & D.C. Richardson (2002) Structure validation by Cα geometry: ϕ/ψ and Cβ deviation. *Proteins: Structure, Function & Genetics.* **50**:437-450

Figure 5: Ramachandran Plot generated by Rampage for the modelled protein, showing percentage of residues lying in the Favoured, Allowed and the Outlier regions.



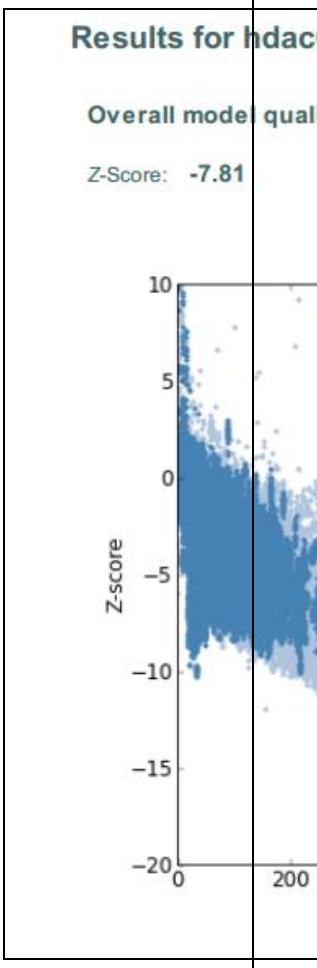


Figure 6: Quality of model assessed using PROSA, the black dot at the centre represents modelled protein.

4.2. Energy Minimization of Protein

The steepest descent algorithm of GROMACS took 588 steps to converge the protein to its minimal energy state. The initial potential energy of the protein was found to be -6.57902 * 10^5 and the final potential energy was found to be -1.0628135 * 10^06. The energy plot was generated using Grace Program which is depicted below and the water from the solvated protein was removed using Rasmol[61, 62].

Figure 7. Plot depicting energy minimization of protein by Gromacs

4.3. Molecular Docking

The active site residues of the protein was identified as HIS611 AND CYS618 through Uniprot. The coordinates of the HIS611 was taken as binding site position. The binding energies and docked conformations of 819 compounds were estimated by docking the compounds to the macromolecule. The table below shows all the compounds along with their top ten binding energies obtained through Autodock Vina.

Table 1. Top ten binding affinities of the docked complexes.

Compound_Id	Top Ten Docked Conformations									
	1	2	3	4	5	6	7	8	9	10
CHEMBL496924	-9.3	-8.6	-8.3	-8.2	-8.2	-8.2	-8.1	-8.1	-8	-8
CHEMBL141082	-9.1	-8.2	-8.2	-8.1	-7.9	-7.9	-7.9	-7.8	-7.8	-7.7
CHEMBL1812335	-9.1	-8.5	-8.5	-8.5	-8.3	-8.3	-8.2	-7.8	-7.8	-7.8
CHEMBL466031	-9.1	-8.2	-8.1	-8	-7.9	-7.8	-7.8	-7.8	-7.6	-7.6
CHEMBL98	-9.1	-8.8	-7.8	-7.8	-7.7	-7.6	-7.6	-7.6	-7.6	-7.3
CHEMBL1487	-8.9	-8.7	-8.6	-8.5	-8.4	-8.3	-8.1	-8.1	-8.1	-8
CHEMBL1164243	-8.8	-8.8	-8.5	-8.5	-8.2	-8.2	-8	-7.9	-7.8	-7.5
CHEMBL468842	-8.7	-8.5	-8.2	-8.2	-8.1	-8.1	-8.1	-8.1	-8	-7.9
CHEMBL481878	-8.7	-8.6	-8.6	-8.5	-8.4	-8.2	-8.1	-8.1	-8	-7.9
CHEMBL2333345	-8.6	-8.3	-8	-8	-7.9	-7.7	-7.6	-7.6	-7.6	-7.5
CHEMBL1214763	-8.5	-8.1	-8.1	-7.9	-7.7	-7.7	-7.7	-7.5	-7.5	-7.5
CHEMBL2047544	-8.5	-7.9	-7.7	-7.5	-7.4	-7.3	-7.2	-7.2	-7.1	-7

CHEMBL567220	-8.5	-8.5	-8.4	-7.8	-7.8	-7.8	-7.7	-7.7	-7.6	-7.5
CHEMBL1797983	-8.4	-7.8	-7.7	-7.7	-7.6	-7.1	-7.1	-7.1	-7.1	-7
CHEMBL363528	-8.4	-7.2	-7.1	-7.1	-7.1	-7.1	-7	-7	-7	-7
CHEMBL466033	-8.4	-8.1	-7.9	-7.9	-7.8	-7.7	-7.7	-7.7	-7.7	-7.7
CHEMBL494645	-8.4	-8.1	-7.9	-7.9	-7.6	-7.5	-7.5	-7.4	-7.3	-7.2
CHEMBL1094707	-8.3	-8.2	-8.1	-8	-7.9	-7.8	-7.8	-7.8	-7.8	-7.7
CHEMBL2158744	-8.3	-6.9	-6.7	-6.6	-6.5	-6.5	-6.4	-6.4	-6.3	-6.3
CHEMBL430060	-8.3	-7.9	-7.7	-7.6	-7.6	-7.5	-7.4	-7.3	-7.3	-7.3
CHEMBL515432	-8.3	-8.2	-7.6	-7.2	-7.1	-7	-6.9	-6.7	-6.7	-6.7
CHEMBL569193	-8.3	-7.8	-7.7	-7.7	-7.7	-7.6	-7.6	-7.6	-7.4	-7.4
CHEMBL1094709	-8.2	-8	-7.9	-7.8	-7.8	-7.8	-7.8	-7.5	-7.5	-7.5
CHEMBL2047699	-8.2	-7.7	-7.7	-7.6	-7.6	-7.6	-7.4	-7.3	-7.1	-7.1
CHEMBL404172	-8.2	-8.1	-8	-8	-8	-7.9	-7.9	-7.9	-7.9	-7.8
CHEMBL99	-8.2	-7.8	-7.3	-7.3	-7.3	-7.3	-7.3	-7.2	-7.2	-6.9
CHEMBL2047539	-8.1	-7.9	-7.7	-7.6	-7.6	-7.3	-7.3	-7.2	-7.2	-7.2
CHEMBL2047541	-8.1	-7.7	-7.5	-7.3	-7.2	-7.2	-7.1	-7	-7	-6.9
CHEMBL1289931	-8	-7.6	-7.4	-7.3	-7.2	-7.2	-7.1	-6.8	-6.7	-6.7
CHEMBL1800382	-8	-7.6	-7.1	-7	-6.9	-6.7	-6.7	-6.5	-6.5	-6.5
CHEMBL2347009	-8	-6.9	-6.7	-6.3	-6.3	-6.2	-6.2	-6.2	-6.2	-6.2
CHEMBL261492	-8	-7.2	-7	-6.9	-6.9	-6.8	-6.8	-6.7	-6.6	-6.6
CHEMBL272980	-8	-7.8	-7.7	-7.5	-7.4	-7.2	-7	-7	-7	-6.9
CHEMBL473891	-8	-7.5	-7.4	-7.4	-7.3	-7.3	-7.3	-7.3	-7.2	-7.2
CHEMBL507716	-8	-8	-7.6	-7.1	-7.1	-7	-7	-7	-6.8	-6.6
CHEMBL519668	-8	-7.5	-7.1	-6.9	-6.9	-6.9	-6.8	-6.6	-6.5	-6.5
CHEMBL567295	-8	-7.4	-7.4	-7.2	-7.2	-7.2	-7.2	-7.1	-7.1	-7.1
CHEMBL1087053	-7.9	-7.7	-7.7	-7.6	-7.5	-7.4	-7.3	-7.3	-7.3	-7.2
CHEMBL1822042	-7.9	-7.8	-7.7	-7.7	-7.6	-7.4	-7.3	-7.2	-7.1	-7.1
CHEMBL2337873	-7.9	-7.8	-7.6	-7.5	-7.5	-7.5	-7.5	-7.5	-7.3	-7.2
CHEMBL2337875	-7.9	-7	-6.9	-6.8	-6.8	-6.6	-6.6	-6.6	-6.6	-6.5

CHEMBL235082	-7.9	-7.8	-7.4	-7.2	-7.2	-7.2	-7.1	-7.1	-7.1	-6.8
CHEMBL259708	-7.9	-7.6	-7.6	-7.6	-7.3	-7.2	-7.1	-7.1	-7	-7
CHEMBL408513	-7.9	-7.1	-7.1	-7	-7	-7	-6.9	-6.9	-6.9	-6.6
CHEMBL466171	-7.9	-7.3	-7.1	-7.1	-7.1	-7	-7	-7	-7	-6.8
CHEMBL475392	-7.9	-7.5	-6.9	-6.8	-6.6	-6.5	-6.3	-6.3	-6.3	-6.3
CHEMBL475820	-7.9	-6.9	-6.7	-6.6	-6.5	-6.5	-6.4	-6.4	-6.4	-6.3
CHEMBL481703	-7.9	-7.5	-7.5	-7.5	-7.3	-6.9	-6.8	-6.7	-6.6	-6.6
CHEMBL492312	-7.9	-7.9	-7.7	-7.6	-7.6	-7.2	-7.2	-7	-6.9	-6.9
CHEMBL493871	-7.9	-7.4	-6.8	-6.6	-6.5	-6.5	-6.5	-6.4	-6.4	-6.4
CHEMBL566641	-7.9	-7.8	-7.8	-7.6	-7.6	-7.5	-7.3	-7.3	-7.2	-7.2
CHEMBL571140	-7.9	-6.9	-6.9	-6.9	-6.8	-6.8	-6.8	-6.7	-6.6	-6.5
CHEMBL571507	-7.9	-7.8	-7.3	-7.1	-7.1	-7	-6.9	-6.9	-6.9	-6.8
CHEMBL1099058	-7.8	-7.5	-7.3	-7.3	-7.3	-7.3	-7.3	-7.2	-7.2	-7.1
CHEMBL1767045	-7.8	-7.3	-7.2	-7.2	-7.2	-7.1	-7	-7	-6.8	-6.8
CHEMBL1800381	-7.8	-7.7	-6.7	-6.6	-6.5	-6.5	-6.5	-6.5	-6.4	-6.4
CHEMBL480729	-7.8	-7.4	-6.9	-6.9	-6.7	-6.6	-6.6	-6.6	-6.4	-6.3
CHEMBL493784	-7.8	-7.4	-7.4	-7.3	-7.3	-7.1	-7.1	-7	-7	-6.9
CHEMBL570490	-7.8	-7.6	-7.4	-7.2	-7.1	-7	-7	-7	-6.9	-6.9
CHEMBL1094792	-7.7	-7.2	-7.2	-7.2	-6.9	-6.8	-6.8	-6.6	-6.6	-6.5
CHEMBL1095400	-7.7	-7.6	-7.3	-7	-6.8	-6.7	-6.7	-6.7	-6.7	-6.6
CHEMBL141885	-7.7	-7.6	-7.4	-7.2	-7.2	-7.2	-7.2	-7.2	-7.1	-7.1
CHEMBL16300	-7.7	-7.3	-7.3	-7.3	-7.2	-7	-6.9	-6.9	-6.9	-6.4
CHEMBL1836142	-7.7	-7.3	-6.9	-6.9	-6.8	-6.5	-6.5	-6.5	-6.4	-6.4
CHEMBL1836144	-7.7	-7.6	-6.7	-6.6	-6.5	-6.5	-6.5	-6.4	-6.4	-6.4
CHEMBL2023526	-7.7	-7	-6.8	-6.7	-6.2	-6.2	-6.2	-6.1	-6	-6
CHEMBL2046456	-7.7	-7.3	-7.1	-7	-6.9	-6.5	-6.4	-6.4	-6.3	-6.3
CHEMBL2152613	-7.7	-7.4	-7.3	-7.3	-7.2	-7.1	-7.1	-7	-7	-7
CHEMBL2158741	-7.7	-7.7	-7.6	-7.6	-7.5	-7.5	-7.5	-7.5	-7.3	-7.3
CHEMBL227119	-7.7	-7.4	-7.1	-7	-6.9	-6.8	-6.4	-6.4	-6.4	-6.4

CHEMBL2333344	-7.7	-7.4	-7.4	-7.4	-7.2	-7.2	-6.8	-6.8	-6.6	-6.6
CHEMBL454671	-7.7	-7.5	-7.4	-7.3	-7.1	-7.1	-6.8	-6.8	-6.8	-6.7
CHEMBL482095	-7.7	-7.7	-7.3	-7	-6.7	-6.7	-6.7	-6.6	-6.6	-6.6
CHEMBL482358	-7.7	-6.9	-6.6	-6.6	-6.5	-6.3	-6.1	-6.1	-6	-6
CHEMBL493315	-7.7	-7.6	-7.6	-7.5	-7.4	-7.3	-7.1	-7	-6.9	-6.8
CHEMBL514511	-7.7	-7.5	-7.4	-7.4	-7.4	-7.3	-7.2	-7.2	-7.1	-7.1
CHEMBL569446	-7.7	-7.2	-7.2	-7.1	-7.1	-7	-6.9	-6.9	-6.9	-6.8
CHEMBL1088734	-7.6	-7.3	-7.2	-7.2	-6.9	-6.8	-6.7	-6.4	-6.3	-6.3
CHEMBL2023527	-7.6	-7.4	-7.3	-7.2	-7.2	-7.1	-7	-6.9	-6.9	-6.8
CHEMBL2047674	-7.6	-6.9	-6.5	-6.5	-6.5	-6.5	-6.5	-6.4	-6.3	-6.3
CHEMBL2047703	-7.6	-7.5	-7.3	-7.1	-7.1	-7	-6.9	-6.7	-6.6	-6.6
CHEMBL2048749	-7.6	-7.5	-7.3	-7.2	-7.2	-7.1	-7.1	-6.9	-6.9	-6.9
CHEMBL2312167	-7.6	-7.4	-7.2	-7	-6.9	-6.9	-6.8	-6.8	-6.7	-6.7
CHEMBL235842	-7.6	-7.3	-7.3	-6.9	-6.7	-6.6	-6.6	-6.5	-6.4	-6.4
CHEMBL466644	-7.6	-6.8	-6.7	-6.7	-6.7	-6.6	-6.5	-6.5	-6.4	-6.4
CHEMBL471042	-7.6	-7.2	-7.2	-7.1	-6.7	-6.6	-6.6	-6.6	-6.6	-6.6
CHEMBL484489	-7.6	-7.1	-7	-6.9	-6.8	-6.7	-6.7	-6.7	-6.6	-6.6
CHEMBL486324	-7.6	-7.3	-7.2	-7.1	-7.1	-7	-6.9	-6.8	-6.8	-6.8
CHEMBL1091474	-7.5	-7.3	-7.2	-7.1	-7	-6.9	-6.9	-6.9	-6.7	-6.5
CHEMBL1094152	-7.5	-7.2	-7.1	-7	-6.7	-6.6	-6.5	-6.4	-6.4	-6.3
CHEMBL1800385	-7.5	-7.3	-7.3	-7.2	-7.2	-7.2	-7	-6.9	-6.9	-6.8
CHEMBL188007	-7.5	-7.3	-7.2	-7.1	-7	-6.9	-6.8	-6.7	-6.6	-6.6
CHEMBL2018301	-7.5	-7	-7	-6.9	-6.9	-6.8	-6.7	-6.6	-6.6	-6.6
CHEMBL213934	-7.5	-6.8	-6.8	-6.8	-6.6	-6.6	-6.6	-6.5	-6.4	-6.4
CHEMBL2153075	-7.5	-7.4	-7.3	-7.2	-7	-7	-7	-6.9	-6.8	-6.7
CHEMBL2170018	-7.5	-7.2	-7.1	-7	-7	-6.9	-6.9	-6.9	-6.9	-6.8
CHEMBL2333343	-7.5	-7	-6.7	-6.7	-6.6	-6.6	-6.5	-6.4	-6.4	-6.4
CHEMBL475203	-7.5	-7.4	-7.2	-7.1	-7	-7	-6.9	-6.9	-6.9	-6.9
CHEMBL569633	-7.5	-7.3	-7.1	-7	-6.9	-6.9	-6.7	-6.6	-6.6	-6.5

CHEMBL86537	-7.5	-7.1	-7	-7	-6.9	-6.9	-6.9	-6.8	-6.8	-6.8
CHEMBL1096981	-7.4	-7.3	-7.1	-7	-7	-6.9	-6.8	-6.7	-6.5	-6.5
CHEMBL1213490	-7.4	-7.3	-7.2	-7.1	-7.1	-6.6	-6.3	-6.3	-6.2	-6.1
CHEMBL1767036	-7.4	-6.8	-6.4	-6.3	-6.2	-6.2	-6.1	-6	-6	-6
CHEMBL1767046	-7.4	-6.9	-6.8	-6.7	-6.5	-6.5	-6.5	-6.5	-6.4	-6.3
CHEMBL2018294	-7.4	-6.4	-6.4	-6.3	-6.3	-6.2	-6.2	-6.2	-6	-5.6
CHEMBL2153071	-7.4	-6.9	-6.4	-6.3	-6.3	-6.2	-6.2	-6.1	-6.1	-6.1
CHEMBL2170017	-7.4	-7.2	-7.1	-7	-6.7	-6.5	-6.4	-6.3	-6.3	-6.3
CHEMBL2177588	-7.4	-7.1	-6.7	-6.6	-6.6	-6.5	-6.5	-6.4	-6.2	-6.1
CHEMBL248486	-7.4	-6.9	-6.8	-6.5	-6.5	-6.4	-6.4	-6.3	-6.1	-6.1
CHEMBL251011	-7.4	-7.4	-7.2	-7	-7	-6.9	-6.8	-6.7	-6.6	-6.4
CHEMBL260653	-7.4	-7.1	-6.8	-6.7	-6.6	-6.6	-6.5	-6.4	-6.3	-6.1
CHEMBL450362	-7.4	-7.3	-7.2	-7	-6.6	-6.5	-6.4	-5.8	-5.8	-5.6
CHEMBL487143	-7.4	-7.3	-7.1	-7	-7	-7	-6.9	-6.9	-6.8	-6.7
CHEMBL525529	-7.4	-7.3	-7	-7	-7	-6.9	-6.9	-6.8	-6.8	-6.7
CHEMBL569174	-7.4	-7.4	-7.3	-7	-6.8	-6.7	-6.7	-6.7	-6.6	-6.6
CHEMBL1095085	-7.3	-7.2	-6.8	-6.7	-6.7	-6.7	-6.7	-6.6	-6.6	-6.4
CHEMBL1099048	-7.3	-7.1	-7.1	-7	-7	-7	-6.9	-6.9	-6.9	-6.7
CHEMBL1165571	-7.3	-7	-6.9	-6.8	-6.7	-6.7	-6.7	-6.6	-6.6	-6.6
CHEMBL1307946	-7.3	-6.7	-6.7	-6.5	-6.4	-6.4	-6.2	-6.2	-6.2	-6.1
CHEMBL1630117	-7.3	-7.1	-7.1	-7	-6.9	-6.8	-6.7	-6.7	-6.7	-6.7
CHEMBL1767030	-7.3	-7.2	-6.9	-6.9	-6.8	-6.8	-6.8	-6.8	-6.8	-6.7
CHEMBL2018300	-7.3	-7	-6.8	-6.8	-6.8	-6.7	-6.7	-6.7	-6.7	-6.7
CHEMBL2018444	-7.3	-7.2	-6.6	-6.4	-6.3	-6.2	-6.1	-6.1	-6.1	-6
CHEMBL2046617	-7.3	-7.2	-7.2	-7.1	-7.1	-7.1	-7	-7	-7	-6.9
CHEMBL2046622	-7.3	-7.1	-7.1	-7.1	-7.1	-7.1	-7	-7	-6.9	-6.8
CHEMBL2047671	-7.3	-7	-6.7	-6.5	-6.4	-6.4	-6.4	-6.3	-6.3	-6.2
CHEMBL2047676	-7.3	-7.2	-7.1	-6.8	-6.8	-6.8	-6.7	-6.7	-6.6	-6.3
CHEMBL2048752	-7.3	-7.2	-7.1	-6.9	-6.9	-6.5	-6.5	-6.4	-6.4	-6.3

CHEMBL2177582	-7.3	-7.2	-6.9	-6.8	-6.8	-6.8	-6.7	-6.6	-6.6	-6.6
CHEMBL263884	-7.3	-7	-7	-7	-6.8	-6.8	-6.8	-6.8	-6.8	-6.8
CHEMBL398420	-7.3	-7.1	-7	-7	-6.9	-6.8	-6.8	-6.7	-6.7	-6.7
CHEMBL398884	-7.3	-7.1	-7.1	-6.8	-6.6	-6.5	-6.4	-6.3	-6.2	-6.2
CHEMBL472250	-7.3	-7.2	-7.1	-7	-6.8	-6.8	-6.6	-6.6	-6.4	-6.4
CHEMBL482280	-7.3	-7.2	-6.9	-6.9	-6.8	-6.8	-6.7	-6.7	-6.6	-6.6
CHEMBL483494	-7.3	-7	-6.6	-6.4	-6.2	-6.1	-6	-5.9	-5.9	-5.9
CHEMBL516915	-7.3	-7.2	-7.1	-7.1	-7.1	-7	-7	-7	-6.9	-6.8
CHEMBL523588	-7.3	-7.2	-7.2	-7.1	-6.7	-6.7	-6.7	-6.6	-6.6	-6.5
CHEMBL554	-7.3	-7	-6.7	-6.7	-6.6	-6.6	-6.6	-6.5	-6.4	-6.2
CHEMBL566873	-7.3	-7.2	-7	-6.9	-6.8	-6.7	-6.6	-6.6	-6.5	-6.4
CHEMBL569211	-7.3	-7.3	-7.2	-7.1	-7.1	-7	-6.9	-6.8	-6.8	-6.7
CHEMBL83747	-7.3	-7.2	-6.9	-6.9	-6.9	-6.8	-6.6	-6.6	-6.5	-6.5
CHEMBL1164225	-7.2	-7.2	-7	-7	-7	-6.7	-6.7	-6.7	-6.6	-6.5
CHEMBL1164241	-7.2	-7	-6.6	-6.5	-6.5	-6.4	-6.4	-6.3	-6.1	-6.1
CHEMBL1243261	-7.2	-7	-6.7	-6.7	-6.6	-6.5	-6.3	-5.9	-5.8	-5.8
CHEMBL1289498	-7.2	-7.1	-7	-6.9	-6.9	-6.9	-6.8	-6.8	-6.8	-6.8
CHEMBL1631910	-7.2	-7.2	-7.2	-7	-7	-6.9	-6.8	-6.8	-6.8	-6.7
CHEMBL1808673	-7.2	-7.2	-6.6	-6.5	-6.5	-6.5	-6.5	-6.4	-6.3	-6.3
CHEMBL197774	-7.2	-7	-6.9	-6.8	-6.7	-6.6	-6.6	-6.5	-6.4	-6.3
CHEMBL2018447	-7.2	-7.1	-6.9	-6.7	-6.6	-6.4	-6.3	-6.3	-6.2	-6.1
CHEMBL2046619	-7.2	-7.1	-7	-7	-6.8	-6.7	-6.6	-6.6	-6.6	-6.5
CHEMBL2046623	-7.2	-7	-6.9	-6.9	-6.8	-6.8	-6.6	-6.5	-6.5	-6.3
CHEMBL2047543	-7.2	-7.1	-6.8	-6.8	-6.7	-6.5	-6.4	-6.2	-6.2	-6.1
CHEMBL2047695	-7.2	-7.2	-6.8	-6.8	-6.8	-6.8	-6.8	-6.7	-6.6	-6.6
CHEMBL2047700	-7.2	-7.1	-7	-7	-6.9	-6.8	-6.8	-6.8	-6.7	-6.7
CHEMBL2170019	-7.2	-7.2	-7.1	-7.1	-7.1	-7	-7	-6.8	-6.7	-6.7
CHEMBL217651	-7.2	-7	-6.6	-6.3	-6.2	-6.2	-6.2	-6.2	-6.2	-6.1
CHEMBL227120	-7.2	-7.2	-7.2	-7.1	-7.1	-7	-7	-6.9	-6.9	-6.9

CHEMBL2337864	-7.2	-7.1	-7.1	-6.8	-6.5	-6	-6	-6	-5.9	-5.9
CHEMBL251144	-7.2	-7.1	-6.9	-6.7	-6.7	-6.6	-6.6	-6.6	-6.5	-6.4
CHEMBL451289	-7.2	-7.1	-6.8	-6.7	-6.3	-6.2	-6.2	-6	-5.9	-5.9
CHEMBL462203	-7.2	-6.6	-6.6	-6.5	-6.5	-6.4	-6.3	-6.3	-6.2	-6.2
CHEMBL462208	-7.2	-6.5	-6.5	-6.4	-6.4	-6.4	-6.3	-6	-6	-6
CHEMBL475095	-7.2	-7.1	-7.1	-6.9	-6.9	-6.9	-6.9	-6.9	-6.8	-6.8
CHEMBL481802	-7.2	-7.1	-7.1	-6.9	-6.9	-6.8	-6.8	-6.6	-6.6	-6.5
CHEMBL490018	-7.2	-7.2	-6.7	-6.7	-6.6	-6.2	-6.2	-6	-5.8	-5.8
CHEMBL496094	-7.2	-6.8	-6.5	-6.5	-6.4	-6.4	-6.4	-6.4	-6.3	-6.1
CHEMBL504161	-7.2	-6.6	-6.5	-6.3	-6.3	-6.3	-6.2	-6.1	-5.9	-5.9
CHEMBL566637	-7.2	-6.6	-6.6	-6.5	-6.4	-6.3	-6.2	-6.1	-6.1	-6
CHEMBL1094077	-7.1	-7	-6.6	-6.5	-6.4	-6.3	-6.2	-6.1	-6	-6
CHEMBL1096033	-7.1	-6.6	-6.6	-6.6	-6.5	-6.5	-6.5	-6.5	-6.5	-6.5
CHEMBL1099049	-7.1	-7.1	-7	-7	-6.8	-6.7	-6.6	-6.6	-6.5	-6.5
CHEMBL1630112	-7.1	-7	-6.7	-6.7	-6.7	-6.7	-6.7	-6.7	-6.6	-6.6
CHEMBL1800380	-7.1	-7	-6.8	-6.8	-6.6	-6.6	-6.6	-6.5	-6.5	-6.4
CHEMBL1836145	-7.1	-6.9	-6.5	-6.2	-6.2	-6.1	-6	-6	-6	-5.9
CHEMBL1938433	-7.1	-7.1	-7	-7	-6.8	-6.7	-6.6	-6.6	-6.5	-6.5
CHEMBL2012815	-7.1	-6.9	-6.9	-6.8	-6.6	-6.5	-6.5	-6.3	-6.3	-6.2
CHEMBL2046613	-7.1	-6.4	-6.4	-6.1	-6	-6	-5.9	-5.9	-5.8	-5.7
CHEMBL2047670	-7.1	-6.9	-6.8	-6.8	-6.8	-6.8	-6.7	-6.6	-6.6	-6.5
CHEMBL2047686	-7.1	-6.3	-6.1	-6.1	-6.1	-6	-5.9	-5.9	-5.8	-5.7
CHEMBL2048750	-7.1	-6.9	-6.1	-5.9	-5.9	-5.7	-5.7	-5.7	-5.6	-5.5
CHEMBL2153074	-7.1	-6.6	-6.5	-6.5	-6.5	-6.4	-6.4	-6.3	-6.3	-6.3
CHEMBL2158743	-7.1	-6.4	-6.2	-6.1	-6	-6	-6	-6	-6	-5.9
CHEMBL2170177	-7.1	-6.9	-6.4	-6.3	-6.2	-6.1	-6	-6	-6	-5.9
CHEMBL2337874	-7.1	-7.1	-7	-6.9	-6.9	-6.9	-6.8	-6.7	-6.7	-6.6
CHEMBL264926	-7.1	-6.9	-6.9	-6.8	-6.7	-6.6	-6.6	-6.5	-6.5	-6.4
CHEMBL27759	-7.1	-6.8	-6.5	-6.5	-6.5	-6.4	-6.4	-6.3	-6.2	-6.2

CHEMBL343448	-7.1	-6.8	-6.6	-6.5	-6.4	-6.2	-6	-5.9	-5.9	-5.9
CHEMBL475293	-7.1	-7	-6.9	-6.9	-6.7	-6.7	-6.5	-6.5	-6.5	-6.5
CHEMBL480005	-7.1	-6.5	-6.5	-6.3	-6.1	-6	-6	-5.9	-5.9	-5.9
CHEMBL481922	-7.1	-6.9	-6.7	-6.7	-6.6	-6.5	-6.5	-6.3	-6.3	-6.3
CHEMBL517076	-7.1	-7	-6.9	-6.8	-6.7	-6.6	-6.6	-6.5	-6.5	-6.5
CHEMBL569674	-7.1	-7	-6.9	-6.9	-6.8	-6.8	-6.7	-6.6	-6.5	-6.5
CHEMBL572175	-7.1	-7	-6.8	-6.7	-6.6	-6.5	-6.5	-6.5	-6.4	-6.4
CHEMBL1099057	-7	-6.7	-6.6	-6.3	-6.2	-6.1	-6.1	-6	-5.9	-5.7
CHEMBL1099065	-7	-6.8	-6.8	-6.7	-6.6	-6.6	-6.5	-6.5	-6.5	-6.4
CHEMBL1164671	-7	-6.6	-6.4	-6.3	-6.3	-6.2	-6.2	-6.2	-6.1	-5.9
CHEMBL139192	-7	-6.7	-6.7	-6.7	-6.6	-6.4	-6.2	-6.2	-6.2	-6.2
CHEMBL1630111	-7	-6.7	-6.7	-6.6	-6.6	-6.6	-6.6	-6.5	-6.5	-6.4
CHEMBL1767047	-7	-6.9	-6.4	-6.3	-6.3	-6.3	-6.2	-6.1	-6.1	-6
CHEMBL1800246	-7	-6.8	-6.7	-6.6	-6.6	-6.6	-6.5	-6.5	-6.5	-6.5
CHEMBL1836042	-7	-6.8	-6.6	-6.5	-6.5	-6.4	-6.4	-6.3	-6.1	-6.1
CHEMBL2012814	-7	-7	-6.7	-6.6	-6.4	-6.3	-6.3	-6.2	-6.1	-6.1
CHEMBL2047681	-7	-6.9	-6.9	-6.9	-6.9	-6.7	-6.7	-6.7	-6.7	-6.7
CHEMBL2047683	-7	-6.7	-6.6	-6.5	-6.5	-6.5	-6.4	-6.3	-6.3	-6.2
CHEMBL2179245	-7	-6.9	-6.4	-6.2	-6.2	-6.1	-6.1	-6	-6	-6
CHEMBL2179616	-7	-6.7	-6.3	-6.2	-6.2	-6	-5.9	-5.9	-5.9	-5.9
CHEMBL221654	-7	-7	-7	-6.9	-6.9	-6.9	-6.9	-6.9	-6.8	-6.7
CHEMBL257973	-7	-6.9	-6.9	-6.9	-6.8	-6.8	-6.7	-6.6	-6.6	-6.5
CHEMBL336935	-7	-6.9	-6.8	-6.7	-6.6	-6.4	-6.3	-6.2	-6.2	-6
CHEMBL462202	-7	-7	-7	-6.7	-6.7	-6.6	-6.6	-6.6	-6.5	-6.5
CHEMBL475391	-7	-6.9	-6.9	-6.6	-6.6	-6.4	-6.3	-6.3	-6.2	-6.2
CHEMBL481805	-7	-6.8	-6.8	-6.7	-6.7	-6.7	-6.7	-6.6	-6.5	-6.4
CHEMBL487533	-7	-6.9	-6.9	-6.8	-6.8	-6.7	-6.4	-6.4	-6.4	-6.3
CHEMBL496703	-7	-6.9	-6.8	-6.7	-6.7	-6.5	-6.5	-6.5	-6.5	-6.5
CHEMBL515109	-7	-6.4	-6.2	-6.2	-6.1	-6	-6	-6	-5.9	-5.9

CHEMBL515256	-7	-6.8	-6.7	-6.7	-6.6	-6.6	-6.5	-6.3	-6.3	-6.2
CHEMBL518957	-7	-7	-6.9	-6.6	-6.4	-6.1	-6	-6	-5.9	-5.9
CHEMBL518961	-7	-6.8	-6.6	-6.4	-6.4	-6.4	-6.4	-6.1	-6.1	-6.1
CHEMBL566092	-7	-6.9	-6.8	-6.5	-6.4	-6.3	-6.3	-6.3	-6.2	-6.2
CHEMBL569812	-7	-6.2	-6	-6	-5.9	-5.8	-5.7	-5.7	-5.6	-5.6
CHEMBL1097369	-6.9	-6.7	-6.7	-6.7	-6.6	-6.5	-6.4	-6.3	-6.3	-6.2
CHEMBL113003	-6.9	-6.8	-6.8	-6.8	-6.7	-6.7	-6.7	-6.6	-6.6	-6.6
CHEMBL1214760	-6.9	-6.6	-6.5	-6.4	-6.3	-6.3	-6.3	-6.2	-6.2	-6.2
CHEMBL1630110	-6.9	-6.8	-6.7	-6.6	-6.6	-6.6	-6.5	-6.5	-6.4	-6.4
CHEMBL1631915	-6.9	-6.7	-6.4	-6.4	-6.3	-6.2	-6.1	-6.1	-6.1	-6
CHEMBL1791401	-6.9	-6.7	-6.6	-6.6	-6.4	-6.3	-6.3	-6.2	-6.2	-6.1
CHEMBL1800379	-6.9	-6.9	-6.8	-6.6	-6.5	-6.3	-6.2	-6	-6	-6
CHEMBL1828920	-6.9	-6.8	-6.8	-6.7	-6.7	-6.7	-6.6	-6.5	-6.5	-6.2
CHEMBL2018297	-6.9	-6.8	-6.7	-6.6	-6.6	-6.6	-6.6	-6.5	-6.5	-6.5
CHEMBL2046616	-6.9	-6.6	-6.5	-6.4	-6.4	-6.4	-6.1	-6.1	-6	-6
CHEMBL2047668	-6.9	-6.5	-6.3	-6.3	-6.1	-6.1	-6.1	-6	-6	-6
CHEMBL406927	-6.9	-6.8	-6.6	-6.6	-6.5	-6.5	-6.4	-6.3	-6.2	-6.2
CHEMBL407959	-6.9	-6.7	-6.7	-6.5	-6.4	-6.4	-6.3	-6.3	-6.3	-6.1
CHEMBL450723	-6.9	-6.6	-6.5	-6.5	-6.5	-6.3	-6.3	-6.2	-6	-6
CHEMBL470225	-6.9	-6.2	-6.2	-6	-6	-5.9	-5.9	-5.9	-5.9	-5.8
CHEMBL474863	-6.9	-6.1	-6.1	-6	-5.9	-5.7	-5.6	-5.6	-5.6	-5.6
CHEMBL481311	-6.9	-6.8	-6.6	-6.5	-6.5	-6.3	-6.2	-6.1	-6.1	-6.1
CHEMBL493782	-6.9	-6.4	-6.2	-6.2	-6.2	-6.2	-6.2	-6.1	-6.1	-6.1
CHEMBL496511	-6.9	-6.6	-6.4	-6.4	-6.3	-6.3	-6.2	-6.1	-6.1	-6.1
CHEMBL515411	-6.9	-6.7	-6.7	-6.6	-6.4	-6.4	-6.3	-6.3	-6.2	-6.1
CHEMBL565289	-6.9	-6.8	-6.7	-6.7	-6.5	-6.5	-6.4	-6.3	-6.3	-6.2
CHEMBL574361	-6.9	-6.9	-6.4	-6	-6	-6	-6	-5.9	-5.9	-5.8
CHEMBL598797	-6.9	-6.7	-6.4	-6.3	-6.1	-6	-5.9	-5.9	-5.7	-5.4
CHEMBL1094158	-6.8	-6.7	-6.7	-6.6	-6.5	-6.5	-6.5	-6.5	-6.4	-6.4

CHEMBL1095764	-6.8	-6.8	-6.8	-6.7	-6.7	-6.7	-6.7	-6.5	-6.3	-6.3
CHEMBL1630116	-6.8	-6.8	-6.7	-6.7	-6.7	-6.7	-6.6	-6.5	-6.3	-6.3
CHEMBL1767038	-6.8	-6.3	-6.3	-6	-5.9	-5.9	-5.8	-5.8	-5.8	-5.8
CHEMBL2047688	-6.8	-6.6	-6.5	-6.4	-6.4	-6.3	-6.2	-6.1	-6.1	-6
CHEMBL2048755	-6.8	-6.6	-6.6	-6.6	-6.5	-6.5	-6.3	-6.2	-6.1	-6.1
CHEMBL2158742	-6.8	-6.7	-6.6	-6.5	-6.5	-6.4	-6.4	-6.4	-6.3	-6.3
CHEMBL2170186	-6.8	-6.5	-6.5	-6.4	-6.4	-6.3	-6.3	-6.3	-6.3	-6.3
CHEMBL2179250	-6.8	-6.6	-6.5	-6.3	-6.2	-6.1	-6.1	-6.1	-6.1	-6.1
CHEMBL2179617	-6.8	-6.5	-6.2	-6	-6	-5.9	-5.9	-5.7	-5.7	-5.7
CHEMBL2204664	-6.8	-6.8	-6.8	-6.7	-6.6	-6.3	-6.3	-6.2	-6.2	-6.1
CHEMBL2312164	-6.8	-6.7	-6.6	-6.6	-6.6	-6.5	-6.4	-6.4	-6.4	-6.4
CHEMBL396097	-6.8	-6.6	-6.6	-6.6	-6.6	-6.6	-6.5	-6.5	-6.5	-6.5
CHEMBL443241	-6.8	-6.7	-6.5	-6.5	-6.4	-6.4	-6.3	-6.1	-6.1	-6.1
CHEMBL468841	-6.8	-6.7	-6.2	-6.1	-6	-5.9	-5.9	-5.9	-5.8	-5.8
CHEMBL469134	-6.8	-6.6	-6.6	-6.4	-6.2	-6.2	-6.1	-6	-6	-6
CHEMBL469275	-6.8	-6.7	-6.6	-6.6	-6.5	-6.5	-6.4	-6.4	-6.4	-6.3
CHEMBL471173	-6.8	-6.4	-6.4	-5.9	-5.8	-5.8	-5.7	-5.5	-5.5	-5.4
CHEMBL480973	-6.8	-6.7	-6.6	-6.6	-6.4	-6.3	-6.3	-6.2	-6.2	-6.2
CHEMBL481018	-6.8	-6.7	-6.7	-6.5	-6.5	-6.4	-6.3	-6.3	-6.3	-6.3
CHEMBL481319	-6.8	-6.6	-6.5	-6.5	-6.4	-6.3	-6.3	-6.3	-6	-6
CHEMBL483893	-6.8	-6.4	-6.4	-6.4	-6.3	-6.2	-6.2	-6.2	-6	-5.9
CHEMBL502752	-6.8	-6.5	-6.4	-6.3	-6.3	-6.3	-6.3	-6.3	-6.3	-6.2
CHEMBL512516	-6.8	-6.8	-6.8	-6.1	-6	-5.9	-5.7	-5.7	-5.6	-5.5
CHEMBL515285	-6.8	-6	-6	-5.9	-5.9	-5.8	-5.8	-5.7	-5.6	-5.6
CHEMBL515452	-6.8	-6.7	-6.5	-6.4	-6.3	-6.3	-6.2	-6.2	-6.2	-6.1
CHEMBL516399	-6.8	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7	-5.7	-5.6	-5.5
CHEMBL521431	-6.8	-6.8	-6.7	-6.7	-6.7	-6.7	-6.6	-6.6	-6.5	-6.5
CHEMBL568151	-6.8	-6.4	-6.4	-6.3	-6.2	-6.1	-6	-6	-5.9	-5.9
CHEMBL570806	-6.8	-6.2	-6.2	-6.2	-6.2	-6.1	-6.1	-6	-6	-6

CHEMBL589918	-6.8	-6.3	-6.2	-6.2	-6.1	-6.1	-6	-6	-6	-6
CHEMBL1088735	-6.7	-6.6	-6.6	-6.5	-6.4	-6.4	-6.3	-6.3	-6.2	-6.2
CHEMBL1098379	-6.7	-6.7	-6.4	-6.4	-6.2	-6.1	-6.1	-6	-5.9	-5.9
CHEMBL1163778	-6.7	-6.5	-6.4	-6.4	-6.3	-6	-6	-5.9	-5.9	-5.9
CHEMBL1164227	-6.7	-6.2	-6.2	-6.1	-6.1	-6.1	-5.9	-5.9	-5.8	-5.8
CHEMBL1164992	-6.7	-6.6	-6.6	-6.1	-6.1	-6.1	-6	-5.9	-5.9	-5.9
CHEMBL1469	-6.7	-6.4	-6.3	-6.1	-6	-5.9	-5.8	-5.8	-5.6	-5.5
CHEMBL1631911	-6.7	-6.6	-6.6	-6.6	-6.5	-6.4	-6.4	-6.3	-6.3	-6.2
CHEMBL1631916	-6.7	-6.7	-6.6	-6.5	-6.2	-6.2	-6.2	-5.9	-5.7	-5.7
CHEMBL1767032	-6.7	-6.3	-6.3	-6.2	-6.2	-6.1	-6.1	-6.1	-6	-6
CHEMBL1798001	-6.7	-6.7	-6.5	-6.5	-6.3	-6.3	-6.3	-6.3	-6.1	-6.1
CHEMBL1800248	-6.7	-6.2	-6.1	-6.1	-6.1	-6.1	-5.9	-5.9	-5.8	-5.8
CHEMBL1800374	-6.7	-6.7	-6.7	-6.6	-6.4	-6.3	-6.3	-6	-6	-5.8
CHEMBL1835671	-6.7	-6.5	-6.4	-6.3	-6.2	-6.1	-6.1	-6	-6	-5.9
CHEMBL2012812	-6.7	-6.2	-5.6	-5.6	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3
CHEMBL2018443	-6.7	-6.5	-5.9	-5.9	-5.8	-5.5	-5.4	-5.3	-5.2	-5.1
CHEMBL2046621	-6.7	-6.2	-6.1	-6.1	-5.9	-5.8	-5.8	-5.7	-5.7	-5.6
CHEMBL2047687	-6.7	-6.7	-6.5	-6.4	-6.3	-6.2	-6.1	-6.1	-6.1	-6
CHEMBL2063395	-6.7	-6.5	-6.4	-6.4	-6.3	-6.2	-6.2	-6	-6	-6
CHEMBL209551	-6.7	-6.1	-6.1	-6	-6	-6	-5.9	-5.9	-5.9	-5.8
CHEMBL2333340	-6.7	-6.5	-6.4	-6.4	-6.3	-6.1	-6.1	-6.1	-6	-5.9
CHEMBL238829	-6.7	-6.6	-6.6	-6.5	-6.5	-6.3	-6.3	-6.2	-6.2	-6
CHEMBL269935	-6.7	-6.6	-6.3	-6.3	-6.2	-6.2	-6.1	-6.1	-6.1	-6
CHEMBL270224	-6.7	-6.6	-6.6	-6.5	-6.3	-6.3	-6.3	-6.3	-6.2	-6.2
CHEMBL402727	-6.7	-6.6	-6.6	-6.4	-6.4	-6.4	-6.2	-6.2	-6.1	-6
CHEMBL471344	-6.7	-6.7	-6.7	-6.6	-6.6	-6.6	-6.6	-6.5	-6.5	-6.5
CHEMBL475042	-6.7	-6.5	-6.5	-6.5	-6.3	-6.3	-6.3	-6.1	-6	-6
CHEMBL479611	-6.7	-6.6	-6.5	-6.5	-6.3	-6.2	-6.2	-6.2	-6.2	-6.2
CHEMBL479842	-6.7	-6.5	-6.3	-6.3	-6.2	-6.1	-6.1	-6	-6	-6

CHEMBL482096	-6.7	-6.6	-6.5	-6.1	-6	-6	-6	-6	-5.9	-5.9
CHEMBL482136	-6.7	-6.6	-6.4	-6.1	-6.1	-6.1	-5.9	-5.9	-5.9	-5.7
CHEMBL487370	-6.7	-6.5	-6.4	-6.4	-6.1	-6.1	-6.1	-6.1	-6	-6
CHEMBL487741	-6.7	-6.4	-6.3	-6.3	-6.1	-6	-5.9	-5.9	-5.9	-5.9
CHEMBL487943	-6.7	-6.7	-6.6	-6.4	-6.4	-6.1	-6.1	-6.1	-6.1	-6
CHEMBL492956	-6.7	-6.6	-6.5	-6.4	-6.3	-6.2	-6.1	-6	-6	-5.9
CHEMBL514671	-6.7	-6	-5.9	-5.9	-5.6	-5.5	-5.4	-5.3	-5.3	-5.2
CHEMBL519491	-6.7	-6.5	-6.3	-6.1	-6.1	-6.1	-6	-6	-6	-5.9
CHEMBL520056	-6.7	-6.7	-6.5	-6.4	-6.4	-6.2	-6.2	-6.1	-6.1	-6.1
CHEMBL564382	-6.7	-6.7	-6.6	-6.5	-6.5	-6.5	-6.5	-6.5	-6.5	-6.4
CHEMBL567457	-6.7	-6.6	-6.5	-6.4	-6.4	-6.3	-6.3	-6.3	-6.2	-6.1
CHEMBL1094085	-6.6	-5.4	-5.4	-5.4	-5.4	-5.2	-5.1	-5.1	-5	-4.9
CHEMBL1094159	-6.6	-6.1	-6.1	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7
CHEMBL1094648	-6.6	-6.4	-6.4	-6.4	-6.4	-6.3	-6.3	-6.3	-6.2	-6.2
CHEMBL1214759	-6.6	-6.4	-5.8	-5.8	-5.8	-5.7	-5.7	-5.6	-5.6	-5.6
CHEMBL1767044	-6.6	-6.6	-6.6	-6.5	-6.3	-6.3	-6.2	-6.1	-6.1	-6.1
CHEMBL1798004	-6.6	-6.6	-6.6	-6.4	-6.2	-6.1	-6.1	-6	-6	-6
CHEMBL1800373	-6.6	-6.5	-6.5	-6.4	-6.3	-6.3	-6.2	-6.2	-6.2	-5.9
CHEMBL1812334	-6.6	-6.1	-6.1	-6.1	-6.1	-6	-6	-6	-5.9	-5.9
CHEMBL1914702	-6.6	-6.2	-6.2	-6.1	-5.9	-5.8	-5.8	-5.8	-5.7	-5.7
CHEMBL2018298	-6.6	-6.5	-6.5	-6.2	-6.1	-6	-6	-6	-6	-5.9
CHEMBL2018303	-6.6	-6.5	-6.4	-6.2	-6	-6	-5.9	-5.9	-5.9	-5.8
CHEMBL2018452	-6.6	-6.4	-6.4	-6.4	-6.3	-6.2	-6.1	-6	-6	-6
CHEMBL2047672	-6.6	-6.5	-6.4	-6.4	-6.2	-6.1	-6	-6	-5.9	-5.9
CHEMBL2047677	-6.6	-6.6	-6.3	-6.2	-6.2	-6.1	-6.1	-6.1	-6	-6
CHEMBL2047704	-6.6	-6.5	-6.5	-6.4	-6.4	-6.3	-6.3	-6.3	-6.2	-6.1
CHEMBL2153072	-6.6	-6.5	-6.4	-6.3	-6.2	-6.2	-6.1	-6	-6	-6
CHEMBL2153079	-6.6	-6.6	-6.5	-6.2	-6.2	-6.1	-6	-6	-5.9	-5.8
CHEMBL227118	-6.6	-6	-5.7	-5.7	-5.6	-5.5	-5.3	-5.2	-5.1	-5.1

CHEMBL2333346	-6.6	-6.4	-6.2	-6.1	-6.1	-6	-6	-6	-5.9	-5.9
CHEMBL2347006	-6.6	-6.6	-6.6	-6.6	-6.4	-6.3	-6.2	-6.2	-6.1	-6.1
CHEMBL2347007	-6.6	-6.5	-6.5	-6.5	-6.5	-6.5	-6.4	-6.4	-6.4	-6.4
CHEMBL242039	-6.6	-6.6	-6.4	-6.4	-6.3	-6.3	-6.2	-6.2	-6.1	-5.9
CHEMBL247654	-6.6	-6.4	-6.4	-6.2	-5.9	-5.8	-5.7	-5.4	-5.4	-5.4
CHEMBL272401	-6.6	-6.5	-6.4	-6.3	-6.2	-6.2	-6.2	-6.1	-6.1	-6.1
CHEMBL360194	-6.6	-6.6	-6.6	-6.5	-6.4	-6.4	-6.3	-6.2	-6.2	-6.2
CHEMBL399494	-6.6	-6.5	-6.4	-6.3	-6.2	-6.1	-6.1	-6	-6	-5.9
CHEMBL427510	-6.6	-6.3	-6.1	-5.9	-5.8	-5.8	-5.7	-5.7	-5.6	-5.6
CHEMBL470470	-6.6	-6.5	-6.4	-6.2	-6.2	-6.1	-6	-5.9	-5.9	-5.8
CHEMBL472631	-6.6	-6.5	-6.3	-6.2	-6.1	-6.1	-5.9	-5.9	-5.9	-5.8
CHEMBL473082	-6.6	-6.5	-6.5	-6.4	-6.3	-6.3	-6.3	-6.3	-6.3	-6.3
CHEMBL473890	-6.6	-6.4	-6.3	-6.2	-6.1	-6	-5.8	-5.8	-5.7	-5.7
CHEMBL479786	-6.6	-6.3	-6.1	-6	-5.9	-5.9	-5.9	-5.8	-5.8	-5.8
CHEMBL481131	-6.6	-6.4	-6.2	-6.1	-6.1	-6	-5.9	-5.9	-5.8	-5.7
CHEMBL482094	-6.6	-6.6	-6.5	-6.3	-6.3	-6.2	-6.1	-6.1	-5.8	-5.7
CHEMBL482271	-6.6	-6.5	-6.5	-6.4	-6.4	-6.4	-6.4	-6.4	-6.3	-6.3
CHEMBL482281	-6.6	-6.6	-6.1	-6.1	-6	-6	-6	-5.8	-5.8	-5.7
CHEMBL485968	-6.6	-6.5	-6.5	-6.4	-6.4	-6.2	-6.1	-6.1	-5.7	-5.7
CHEMBL488747	-6.6	-6.3	-6.2	-6.1	-6	-6	-6	-6	-6	-5.9
CHEMBL497332	-6.6	-6.3	-6.2	-6.1	-6	-5.9	-5.7	-5.7	-5.7	-5.6
CHEMBL509445	-6.6	-6.5	-6.4	-6.4	-6.3	-6.3	-6.1	-6.1	-6.1	-6
CHEMBL513160	-6.6	-6.3	-6.2	-6.1	-6.1	-6.1	-6	-5.8	-5.8	-5.8
CHEMBL520781	-6.6	-6.3	-6.2	-6	-6	-5.9	-5.9	-5.8	-5.7	-5.7
CHEMBL523684	-6.6	-6.3	-6.3	-6.1	-6.1	-6.1	-6	-5.8	-5.8	-5.8
CHEMBL524024	-6.6	-6.3	-6.2	-6.1	-6.1	-6	-5.9	-5.9	-5.8	-5.8
CHEMBL568955	-6.6	-6.6	-6.4	-6.3	-6.3	-6.3	-6.3	-6.3	-6.2	-6.1
CHEMBL569192	-6.6	-6.6	-6.4	-6.4	-6.3	-6.2	-6	-5.9	-5.8	-5.8
CHEMBL592719	-6.6	-6.5	-6.4	-6.4	-6.4	-6.4	-6.2	-6.1	-6.1	-6

CHEMBL1095135	-6.5	-6.4	-6.3	-6.1	-6.1	-6	-5.9	-5.9	-5.8	-5.8
CHEMBL1095450	-6.5	-5.8	-5.5	-5.5	-5.2	-5.1	-4.9	-4.6	-4.5	-4.4
CHEMBL1096982	-6.5	-6	-5.9	-5.9	-5.8	-5.8	-5.8	-5.8	-5.7	-5.7
CHEMBL1214762	-6.5	-6.4	-6.3	-6.2	-6.1	-6.1	-6	-5.9	-5.9	-5.8
CHEMBL156887	-6.5	-6.4	-6	-5.7	-5.7	-5.6	-5.6	-5.6	-5.5	-5.5
CHEMBL1631917	-6.5	-6.4	-6.4	-6.1	-5.7	-5.5	-5.4	-5.2	-5.2	-4.9
CHEMBL1668018	-6.5	-6.5	-6.4	-6.3	-6.3	-6.3	-6.3	-6.2	-6.1	-6.1
CHEMBL1767029	-6.5	-6.3	-6	-5.8	-5.6	-5.5	-5.4	-5.4	-5.3	-5.3
CHEMBL1800247	-6.5	-6.4	-6.4	-6.3	-6.3	-6.2	-6.2	-6.1	-6.1	-6.1
CHEMBL1801250	-6.5	-5.9	-5.8	-5.7	-5.7	-5.7	-5.7	-5.7	-5.6	-5.6
CHEMBL2012811	-6.5	-6.5	-6.3	-6.3	-6.2	-6.2	-6.2	-6.2	-6.2	-6.1
CHEMBL2018441	-6.5	-6.3	-6.3	-6.2	-5.9	-5.9	-5.9	-5.8	-5.7	-5.7
CHEMBL2018442	-6.5	-6.1	-6	-6	-6	-6	-5.9	-5.9	-5.9	-5.9
CHEMBL2047701	-6.5	-6.4	-6.3	-6.3	-6.2	-6.2	-6.2	-6	-6	-6
CHEMBL2153070	-6.5	-6.4	-6.4	-6.2	-6	-5.8	-5.8	-5.7	-5.7	-5.7
CHEMBL2153073	-6.5	-6.5	-6.4	-6.4	-6.4	-6.4	-6.3	-6.3	-6.3	-6.3
CHEMBL227170	-6.5	-6.2	-6.2	-6.1	-6.1	-6	-5.9	-5.9	-5.8	-5.8
CHEMBL2312168	-6.5	-6.5	-6.5	-6.3	-6.2	-6.1	-6	-6	-5.9	-5.9
CHEMBL235210	-6.5	-6	-6	-6	-5.9	-5.9	-5.9	-5.8	-5.8	-5.8
CHEMBL255805	-6.5	-5.8	-5.6	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3	-5.3
CHEMBL259434	-6.5	-6.1	-5.9	-5.9	-5.9	-5.8	-5.8	-5.8	-5.8	-5.7
CHEMBL406734	-6.5	-6.5	-6.3	-6.3	-6.3	-6.2	-6.1	-6.1	-6.1	-6
CHEMBL445518	-6.5	-6.3	-6.3	-6.3	-6.3	-6.2	-6	-5.9	-5.9	-5.8
CHEMBL446512	-6.5	-6.1	-6.1	-6	-6	-5.9	-5.8	-5.8	-5.7	-5.7
CHEMBL462146	-6.5	-6.4	-6.3	-6.3	-6.2	-6.1	-6.1	-6.1	-6	-5.9
CHEMBL468513	-6.5	-6.5	-6.5	-6.5	-6.4	-6.4	-6.4	-6.4	-6.3	-6.3
CHEMBL474046	-6.5	-6.2	-6.2	-5.8	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5
CHEMBL493749	-6.5	-5.8	-5.6	-5.6	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4
CHEMBL514478	-6.5	-6.4	-6.1	-6.1	-6	-6	-6	-5.7	-5.6	-5.5

CHEMBL566824	-6.5	-6.4	-6.3	-6.2	-6.1	-5.9	-5.9	-5.6	-5.4	-5.3
CHEMBL570041	-6.5	-6.3	-6.3	-6.3	-6.1	-6.1	-6.1	-6	-6	-6
CHEMBL585939	-6.5	-6.2	-6.2	-6.1	-6.1	-6.1	-6	-5.9	-5.8	-5.8
CHEMBL609583	-6.5	-5.5	-5.4	-5.4	-5.3	-5.1	-5	-5	-5	-4.9
CHEMBL96051	-6.5	-6.3	-6.2	-6.1	-5.9	-5.9	-5.8	-5.7	-5.7	-5.7
CHEMBL1093335	-6.4	-6.4	-6.1	-6.1	-6	-5.8	-5.7	-5.7	-5.7	-5.7
CHEMBL1095124	-6.4	-5.9	-5.9	-5.9	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5
CHEMBL1096034	-6.4	-6.1	-6	-6	-6	-5.9	-5.9	-5.8	-5.8	-5.7
CHEMBL1096985	-6.4	-6.4	-6.3	-6.2	-6.2	-6	-6	-5.9	-5.9	-5.9
CHEMBL1165164	-6.4	-6.3	-6.2	-6.2	-6.2	-6.1	-6.1	-6	-6	-6
CHEMBL138090	-6.4	-6	-5.9	-5.9	-5.8	-5.8	-5.7	-5.6	-5.6	-5.6
CHEMBL1630109	-6.4	-6.4	-6.2	-6.1	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7
CHEMBL1767035	-6.4	-6.3	-6.2	-6.1	-6.1	-6	-6	-5.9	-5.8	-5.8
CHEMBL1767037	-6.4	-6.3	-6.2	-6.2	-6.1	-5.9	-5.8	-5.7	-5.7	-5.6
CHEMBL1798006	-6.4	-6.2	-6.1	-5.9	-5.8	-5.8	-5.8	-5.7	-5.6	-5.6
CHEMBL1808674	-6.4	-6.1	-5.9	-5.8	-5.7	-5.7	-5.6	-5.5	-5.5	-5.5
CHEMBL2018295	-6.4	-6.1	-6.1	-6	-5.9	-5.9	-5.9	-5.8	-5.8	-5.8
CHEMBL2046608	-6.4	-6.4	-6.3	-6.3	-6.1	-6.1	-6.1	-5.9	-5.9	-5.9
CHEMBL2046615	-6.4	-6.3	-6.3	-6.3	-6.1	-6.1	-6	-5.9	-5.9	-5.9
CHEMBL2153076	-6.4	-6.3	-6.1	-6	-6	-5.9	-5.9	-5.9	-5.8	-5.8
CHEMBL2178345	-6.4	-6	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7	-5.6	-5.6
CHEMBL2337869	-6.4	-6.1	-5.9	-5.9	-5.9	-5.8	-5.7	-5.7	-5.7	-5.6
CHEMBL243997	-6.4	-6.4	-6.2	-6.2	-6.2	-6.1	-6.1	-6.1	-6.1	-6
CHEMBL402363	-6.4	-5.9	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5	-5.4
CHEMBL474097	-6.4	-6.4	-6.2	-6.2	-6.1	-6.1	-6	-5.9	-5.9	-5.9
CHEMBL475861	-6.4	-6.3	-6.2	-6.1	-5.8	-5.8	-5.6	-5.6	-5.5	-5.4
CHEMBL479970	-6.4	-6.3	-6.2	-6.2	-6.2	-6.1	-6.1	-6.1	-6	-6
CHEMBL479971	-6.4	-6	-5.6	-5.6	-5.6	-5.6	-5.4	-5.4	-5.3	-5.3
CHEMBL487107	-6.4	-6.3	-5.7	-5.5	-5.4	-5.4	-5.4	-5.4	-5.4	-5.3

CHEMBL487615	-6.4	-6.3	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7	-5.6	-5.4
CHEMBL493347	-6.4	-6.4	-6.3	-6.2	-6.1	-6.1	-6.1	-6.1	-6.1	-6
CHEMBL493872	-6.4	-6.3	-6.3	-6.3	-6.3	-6.2	-6.2	-6.2	-6.1	-6
CHEMBL494331	-6.4	-5.9	-5.8	-5.3	-5.1	-5.1	-5	-5	-5	-4.9
CHEMBL511715	-6.4	-6.2	-6.2	-6	-6	-5.9	-5.7	-5.7	-5.6	-5.6
CHEMBL511749	-6.4	-6.2	-6.2	-6.1	-6.1	-6.1	-6.1	-6.1	-6	-6
CHEMBL524193	-6.4	-6.3	-6.2	-6.2	-6	-5.9	-5.9	-5.8	-5.8	-5.7
CHEMBL1091475	-6.3	-6.2	-6.1	-6.1	-6	-6	-6	-5.8	-5.8	-5.8
CHEMBL1094710	-6.3	-6.1	-5.7	-5.6	-5.4	-5.3	-5.2	-5.2	-5.1	-5.1
CHEMBL1095119	-6.3	-6.2	-6.1	-6.1	-6.1	-6	-6	-6	-6	-5.9
CHEMBL1095719	-6.3	-5.7	-5.6	-5.6	-5.5	-5.4	-5.3	-5.2	-5.1	-5
CHEMBL1097981	-6.3	-6.2	-6.2	-6	-5.9	-5.7	-5.6	-5.6	-5.5	-5.5
CHEMBL1098042	-6.3	-6.2	-6.2	-6.1	-6.1	-6.1	-6	-6	-5.9	-5.9
CHEMBL115468	-6.3	-5.9	-5.9	-5.8	-5.7	-5.6	-5.5	-5.5	-5.5	-5.4
CHEMBL1164226	-6.3	-6.3	-6.1	-6	-6	-6	-6	-5.9	-5.9	-5.9
CHEMBL1243289	-6.3	-5.8	-5.6	-5.4	-5.2	-4.6	-4.5	-4.4	-4.4	-4.4
CHEMBL1722433	-6.3	-6.2	-6.2	-5.8	-5.7	-5.7	-5.5	-5.4	-5.3	-5.2
CHEMBL1800243	-6.3	-5.9	-5.9	-5.7	-5.7	-5.7	-5.6	-5.5	-5.5	-5.5
CHEMBL180911	-6.3	-6.3	-6.1	-6	-6	-6	-6	-5.9	-5.9	-5.9
CHEMBL2012818	-6.3	-6	-5.9	-5.9	-5.7	-5.6	-5.6	-5.6	-5.6	-5.5
CHEMBL2018299	-6.3	-6.2	-6	-5.9	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7
CHEMBL2023529	-6.3	-6.2	-6.2	-6.1	-6	-5.9	-5.8	-5.8	-5.7	-5.7
CHEMBL2023530	-6.3	-6.2	-5.8	-5.8	-5.7	-5.7	-5.6	-5.6	-5.6	-5.4
CHEMBL2047673	-6.3	-6.1	-6	-6	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7
CHEMBL2047675	-6.3	-5.7	-5.6	-5.6	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3
CHEMBL2063396	-6.3	-6.2	-6	-6	-5.9	-5.8	-5.8	-5.8	-5.8	-5.8
CHEMBL2093007	-6.3	-5.9	-5.9	-5.7	-5.7	-5.7	-5.5	-5.5	-5.4	-5.4
CHEMBL2337862	-6.3	-5.9	-5.9	-5.7	-5.5	-5.4	-5.3	-5.3	-5.3	-5.2
CHEMBL2337865	-6.3	-5.9	-5.7	-5.6	-5.6	-5.6	-5.6	-5.4	-5.4	-5.4

CHEMBL2337868	-6.3	-6.3	-6.3	-6.3	-6.3	-6.2	-6.1	-6.1	-6.1	-6.1
CHEMBL235674	-6.3	-6.2	-6.1	-6.1	-6.1	-5.9	-5.9	-5.9	-5.8	-5.8
CHEMBL255714	-6.3	-5.9	-5.8	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5
CHEMBL337584	-6.3	-6.1	-6	-6	-5.9	-5.9	-5.8	-5.8	-5.8	-5.6
CHEMBL389687	-6.3	-6.2	-6.1	-6.1	-6	-5.9	-5.9	-5.7	-5.6	-5.6
CHEMBL437029	-6.3	-6	-6	-5.8	-5.7	-5.5	-5.5	-5.5	-5.5	-5.4
CHEMBL474015	-6.3	-6.3	-6.2	-6.1	-6	-5.9	-5.8	-5.8	-5.7	-5.7
CHEMBL481297	-6.3	-6.2	-6.1	-5.8	-5.8	-5.8	-5.8	-5.8	-5.8	-5.7
CHEMBL483495	-6.3	-5.7	-5.6	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3	-5.3
CHEMBL485967	-6.3	-6.2	-6.1	-6	-5.9	-5.9	-5.6	-5.6	-5.6	-5.6
CHEMBL511432	-6.3	-6.1	-6.1	-6.1	-5.8	-5.8	-5.8	-5.7	-5.7	-5.6
CHEMBL519746	-6.3	-5.9	-5.8	-5.7	-5.6	-5.3	-5.3	-5.3	-5.2	-5.2
CHEMBL568958	-6.3	-6.3	-6.1	-6	-6	-5.9	-5.9	-5.9	-5.7	-5.7
CHEMBL598363	-6.3	-6	-6	-5.9	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7
CHEMBL1076939	-6.2	-6.1	-6.1	-5.7	-5.5	-5.4	-5.4	-5.2	-5.1	-5
CHEMBL1088736	-6.2	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4
CHEMBL1093033	-6.2	-6.1	-5.9	-5.5	-5.4	-5.4	-5.4	-5.3	-5.2	-5.1
CHEMBL115011	-6.2	-6.1	-6	-5.9	-5.9	-5.9	-5.8	-5.7	-5.6	-5.6
CHEMBL1165293	-6.2	-6.1	-6	-5.9	-5.8	-5.8	-5.8	-5.7	-5.7	-5.6
CHEMBL1798007	-6.2	-6.2	-5.8	-5.5	-5.5	-5.4	-5.3	-5.3	-5.3	-5.2
CHEMBL2018302	-6.2	-5.8	-5.7	-5.7	-5.7	-5.5	-5.4	-5.4	-5.3	-5.2
CHEMBL2023528	-6.2	-5.8	-5.7	-5.7	-5.6	-5.5	-5.5	-5.5	-5.4	-5.4
CHEMBL2047678	-6.2	-6.2	-6.1	-6.1	-5.9	-5.8	-5.8	-5.8	-5.8	-5.8
CHEMBL2179246	-6.2	-6	-6	-6	-5.9	-5.7	-5.7	-5.7	-5.6	-5.6
CHEMBL2179249	-6.2	-6.2	-6.1	-5.9	-5.7	-5.7	-5.6	-5.6	-5.6	-5.5
CHEMBL2179619	-6.2	-6.1	-6.1	-6	-5.9	-5.9	-5.9	-5.9	-5.9	-5.8
CHEMBL236678	-6.2	-6	-5.7	-5.7	-5.7	-5.6	-5.6	-5.6	-5.6	-5.5
CHEMBL247217	-6.2	-5.8	-5.6	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3
CHEMBL253868	-6.2	-6.2	-6.2	-6.2	-6.1	-6.1	-6.1	-6.1	-6	-6

CHEMBL256440	-6.2	-6.1	-6.1	-6	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7
CHEMBL363750	-6.2	-6.1	-6	-6	-5.8	-5.7	-5.6	-5.6	-5.6	-5.5
CHEMBL379049	-6.2	-6.2	-6.2	-5.7	-5.7	-5.5	-5.5	-5.3	-5.3	-5.3
CHEMBL401837	-6.2	-6.2	-6	-6	-6	-5.9	-5.9	-5.9	-5.8	-5.8
CHEMBL454438	-6.2	-6.2	-6.2	-6.1	-6	-5.9	-5.9	-5.9	-5.8	-5.7
CHEMBL455735	-6.2	-5.9	-5.6	-5.6	-5.6	-5.5	-5.4	-5.3	-5.3	-5.2
CHEMBL467678	-6.2	-6.1	-5.9	-5.7	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3
CHEMBL469274	-6.2	-6.2	-6	-5.9	-5.9	-5.7	-5.6	-5.6	-5.6	-5.6
CHEMBL471044	-6.2	-5.9	-5.8	-5.7	-5.6	-5.6	-5.6	-5.6	-5.6	-5.6
CHEMBL474001	-6.2	-5.5	-5.4	-5.4	-5.3	-5.2	-5.2	-5.2	-5.2	-5.2
CHEMBL474446	-6.2	-5.9	-5.9	-5.9	-5.7	-5.7	-5.6	-5.5	-5.4	-5.4
CHEMBL475101	-6.2	-5.8	-5.7	-5.5	-5.5	-5.4	-5.4	-5.4	-5.4	-5.3
CHEMBL481136	-6.2	-6.1	-6.1	-5.9	-5.8	-5.7	-5.6	-5.6	-5.6	-5.5
CHEMBL481148	-6.2	-6	-5.9	-5.9	-5.8	-5.7	-5.7	-5.7	-5.7	-5.6
CHEMBL482765	-6.2	-6.1	-6	-5.8	-5.8	-5.8	-5.8	-5.8	-5.8	-5.7
CHEMBL485514	-6.2	-6	-5.9	-5.9	-5.9	-5.8	-5.7	-5.7	-5.7	-5.7
CHEMBL490067	-6.2	-6	-5.8	-5.6	-5.6	-5.6	-5.5	-5.4	-5.4	-5.4
CHEMBL493785	-6.2	-6.1	-5.8	-5.8	-5.8	-5.7	-5.7	-5.7	-5.7	-5.6
CHEMBL504040	-6.2	-5.7	-5.7	-5.6	-5.5	-5.2	-5.2	-5.2	-5.1	-5
CHEMBL514351	-6.2	-6.1	-5.7	-5.7	-5.4	-5.4	-5.3	-5.3	-5.3	-5.2
CHEMBL517997	-6.2	-5.9	-5.9	-5.7	-5.6	-5.6	-5.6	-5.6	-5.5	-5.4
CHEMBL519739	-6.2	-6.2	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5	-5.5
CHEMBL55895	-6.2	-5.9	-5.6	-5.6	-5.4	-5.4	-5.4	-5.4	-5.3	-5.2
CHEMBL582926	-6.2	-6.1	-6.1	-6	-6	-6	-5.8	-5.7	-5.7	-5.6
CHEMBL594544	-6.2	-5.9	-5.7	-5.7	-5.7	-5.6	-5.6	-5.5	-5.4	-5.4
CHEMBL1095076	-6.1	-6.1	-6	-6	-5.9	-5.9	-5.8	-5.7	-5.6	-5.6
CHEMBL1095118	-6.1	-6	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7	-5.6
CHEMBL1095437	-6.1	-6	-6	-5.8	-5.8	-5.7	-5.6	-5.6	-5.6	-5.4
CHEMBL1095765	-6.1	-5.9	-5.9	-5.9	-5.8	-5.7	-5.6	-5.4	-5.3	-5.3

CHEMBL1096432	-6.1	-5.9	-5.9	-5.9	-5.7	-5.6	-5.6	-5.6	-5.5	-5.4
CHEMBL1097761	-6.1	-5.7	-5.5	-5.4	-5.4	-5.3	-5.2	-5.2	-5.1	-5
CHEMBL1098067	-6.1	-5.7	-5.6	-5.6	-5.6	-5.5	-5.4	-5.4	-5.3	-5.3
CHEMBL1164244	-6.1	-6.1	-6	-5.7	-5.7	-5.7	-5.6	-5.6	-5.5	-5.4
CHEMBL1290142	-6.1	-6	-5.9	-5.9	-5.9	-5.7	-5.6	-5.6	-5.5	-5.5
CHEMBL152665	-6.1	-5.9	-5.8	-5.7	-5.6	-5.5	-5.5	-5.5	-5.4	-5.3
CHEMBL1672332	-6.1	-6	-5.8	-5.8	-5.7	-5.7	-5.7	-5.6	-5.6	-5.5
CHEMBL1767040	-6.1	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5	-5.4	-5.4	-5.3
CHEMBL1798005	-6.1	-6	-6	-5.9	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7
CHEMBL1800375	-6.1	-6	-5.9	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7
CHEMBL1822043	-6.1	-6	-5.8	-5.5	-5.4	-5.3	-5.1	-5.1	-5	-5
CHEMBL2018450	-6.1	-6	-5.9	-5.9	-5.8	-5.8	-5.7	-5.6	-5.6	-5.5
CHEMBL2046620	-6.1	-5.9	-5.7	-5.5	-5.4	-5.3	-5.3	-5.1	-5.1	-5.1
CHEMBL2047669	-6.1	-5.8	-5.7	-5.7	-5.6	-5.6	-5.6	-5.5	-5.5	-5.5
CHEMBL2047680	-6.1	-6.1	-5.6	-5.2	-5	-4.9	-4.9	-4.9	-4.9	-4.6
CHEMBL2047690	-6.1	-5.7	-5.6	-5.2	-5.2	-5.1	-5.1	-5.1	-5.1	-5
CHEMBL2153078	-6.1	-5.9	-5.7	-5.6	-5.4	-5.2	-5	-4.8	-4.6	-4.6
CHEMBL2179244	-6.1	-5.8	-5.7	-5.7	-5.7	-5.6	-5.5	-5.5	-5.5	-5.5
CHEMBL2179248	-6.1	-6	-5.8	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5	-5.5
CHEMBL471041	-6.1	-5.9	-5.9	-5.8	-5.8	-5.7	-5.6	-5.6	-5.5	-5.5
CHEMBL473825	-6.1	-6.1	-6.1	-6.1	-6	-6	-5.9	-5.9	-5.8	-5.8
CHEMBL475102	-6.1	-6.1	-5.8	-5.8	-5.8	-5.8	-5.8	-5.8	-5.8	-5.7
CHEMBL475796	-6.1	-6	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7	-5.6	-5.6
CHEMBL482075	-6.1	-5.9	-5.7	-5.7	-5.7	-5.6	-5.6	-5.5	-5.4	-5.4
CHEMBL482137	-6.1	-6.1	-6.1	-6	-6	-6	-5.9	-5.9	-5.8	-5.7
CHEMBL483693	-6.1	-5.9	-5.8	-5.8	-5.7	-5.6	-5.5	-5.5	-5.4	-5.3
CHEMBL487742	-6.1	-6	-5.9	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5
CHEMBL497123	-6.1	-6.1	-5.6	-5.5	-5.5	-5.5	-5.5	-5.5	-5.5	-5.4
CHEMBL519134	-6.1	-5.9	-5.9	-5.8	-5.7	-5.7	-5.6	-5.6	-5.5	-5.4

CHEMBL521355	-6.1	-5.9	-5.8	-5.7	-5.7	-5.6	-5.5	-5.5	-5.3	-5.3
CHEMBL1091815	-6	-5.8	-5.6	-5.5	-5.5	-5.5	-5.4	-5.4	-5.3	-5.3
CHEMBL1094794	-6	-5.9	-5.8	-5.8	-5.8	-5.5	-5.5	-5.4	-5.4	-5.3
CHEMBL138626	-6	-5.9	-5.9	-5.8	-5.7	-5.7	-5.6	-5.6	-5.6	-5.5
CHEMBL1630107	-6	-6	-5.7	-5.6	-5.6	-5.5	-5.5	-5.3	-5.3	-5.1
CHEMBL1800241	-6	-6	-5.9	-5.9	-5.8	-5.8	-5.8	-5.7	-5.6	-5.6
CHEMBL1822046	-6	-5.8	-5.7	-5.4	-5.2	-5	-5	-5	-4.9	-4.9
CHEMBL1923808	-6	-6	-6	-5.8	-5.8	-5.7	-5.5	-5.5	-5.5	-5.5
CHEMBL2012817	-6	-6	-6	-5.9	-5.7	-5.6	-5.5	-5.5	-5.4	-5.4
CHEMBL2018296	-6	-5.9	-5.9	-5.7	-5.4	-5.4	-5.3	-5.3	-5.3	-5.2
CHEMBL2018449	-6	-6	-5.9	-5.8	-5.8	-5.7	-5.7	-5.6	-5.6	-5.6
CHEMBL2046611	-6	-6	-6	-6	-5.9	-5.9	-5.8	-5.8	-5.8	-5.8
CHEMBL2047540	-6	-5.8	-5.7	-5.7	-5.6	-5.6	-5.5	-5.4	-5.4	-5.4
CHEMBL2047689	-6	-5.9	-5.8	-5.7	-5.6	-5.6	-5.4	-5.4	-5.4	-5.3
CHEMBL2047691	-6	-5.9	-5.7	-5.7	-5.7	-5.6	-5.5	-5.5	-5.4	-5.4
CHEMBL2047696	-6	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7	-5.7	-5.7	-5.7
CHEMBL2153077	-6	-6	-6	-6	-5.9	-5.9	-5.8	-5.7	-5.7	-5.5
CHEMBL2178344	-6	-5.4	-5.3	-5	-5	-4.8	-4.8	-4.7	-4.6	-4.6
CHEMBL2333338	-6	-5.9	-5.9	-5.9	-5.8	-5.7	-5.5	-5.5	-5.4	-5.4
CHEMBL409526	-6	-5.9	-5.9	-5.9	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7
CHEMBL455455	-6	-5.7	-5.7	-5.7	-5.5	-5.5	-5.5	-5.4	-5.3	-5.2
CHEMBL462209	-6	-5.4	-5.2	-4.9	-4.6	-4.5	-4.5	-4.3	-4.3	-4.1
CHEMBL470843	-6	-5.7	-5.5	-5.5	-5.4	-5.3	-5.3	-5.3	-5.2	-5.2
CHEMBL475307	-6	-5.8	-5.8	-5.7	-5.5	-5.5	-5.5	-5.5	-5.4	-5.4
CHEMBL481955	-6	-5.9	-5.9	-5.9	-5.9	-5.8	-5.7	-5.7	-5.7	-5.5
CHEMBL482270	-6	-6	-6	-6	-5.9	-5.9	-5.9	-5.7	-5.6	-5.6
CHEMBL512043	-6	-5.9	-5.8	-5.8	-5.7	-5.7	-5.6	-5.6	-5.6	-5.6
CHEMBL512644	-6	-5.9	-5.7	-5.7	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5
CHEMBL515258	-6	-5.9	-5.8	-5.7	-5.7	-5.7	-5.7	-5.6	-5.6	-5.5

CHEMBL516218	-6	-5.7	-5.5	-5.5	-5.5	-5.4	-5.3	-5.2	-5.2	-5.1
CHEMBL569447	-6	-5.9	-5.8	-5.8	-5.7	-5.5	-5.5	-5.3	-5.3	-5.3
CHEMBL569946	-6	-5.7	-5.7	-5.7	-5.6	-5.5	-5.5	-5.3	-5.3	-5.3
CHEMBL941	-6	-5.7	-5.4	-5.4	-5.4	-5.3	-5.3	-5.3	-5.2	-5.2
CHEMBL1164212	-5.9	-5.8	-5.7	-5.7	-5.7	-5.7	-5.3	-5.3	-5.3	-5.3
CHEMBL1767042	-5.9	-5.9	-5.8	-5.7	-5.6	-5.6	-5.5	-5.4	-5.4	-5.3
CHEMBL1800242	-5.9	-5.9	-5.8	-5.6	-5.6	-5.5	-5.5	-5.4	-5.4	-5.3
CHEMBL1800384	-5.9	-5.9	-5.9	-5.9	-5.8	-5.8	-5.8	-5.7	-5.7	-5.7
CHEMBL2012813	-5.9	-5.7	-5.6	-5.6	-5.6	-5.3	-5.3	-5.3	-5.2	-5.2
CHEMBL2048746	-5.9	-5.9	-5.8	-5.7	-5.7	-5.6	-5.5	-5.4	-5.4	-5.4
CHEMBL2178342	-5.9	-5.9	-5.8	-5.7	-5.6	-5.3	-5.2	-5.2	-5.1	-4.9
CHEMBL2179247	-5.9	-5.9	-5.7	-5.7	-5.7	-5.5	-5.5	-5.5	-5.4	-5.4
CHEMBL235300	-5.9	-5.7	-5.6	-5.6	-5.5	-5.3	-5.2	-5.2	-5.1	-5.1
CHEMBL253308	-5.9	-5.7	-5.6	-5.5	-5.5	-5.2	-5.2	-5.2	-5.2	-5.2
CHEMBL257972	-5.9	-5.9	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5	-5.5	-5.4
CHEMBL356066	-5.9	-5.7	-5.4	-5.4	-5.3	-5.2	-5.1	-5.1	-5.1	-5.1
CHEMBL388710	-5.9	-5.7	-5.6	-5.5	-5.5	-5.5	-5.5	-5.5	-5.5	-5.4
CHEMBL461333	-5.9	-5.8	-5.7	-5.6	-5.6	-5.6	-5.5	-5.5	-5.5	-5.4
CHEMBL462223	-5.9	-5.8	-5.8	-5.7	-5.7	-5.7	-5.6	-5.6	-5.6	-5.6
CHEMBL467793	-5.9	-5.9	-5.8	-5.8	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3
CHEMBL481538	-5.9	-5.7	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5	-5.4
CHEMBL483892	-5.9	-5.3	-5.2	-5.2	-5.2	-5.2	-5.1	-5	-5	-5
CHEMBL494138	-5.9	-5.9	-5.9	-5.9	-5.9	-5.8	-5.8	-5.8	-5.7	-5.7
CHEMBL514485	-5.9	-5.8	-5.6	-5.6	-5.5	-5.4	-5.4	-5.3	-5.3	-5.2
CHEMBL519738	-5.9	-5.9	-5.7	-5.5	-5.4	-5.1	-5.1	-5	-4.9	-4.7
CHEMBL566817	-5.9	-5.6	-4.6	-4.6	-4.4	-4.3	-4.1	-4.1	-3.9	-3.9
CHEMBL569288	-5.9	-5.6	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3	-5.1	-5.1
CHEMBL570589	-5.9	-5.7	-5.6	-5.5	-5.4	-5.1	-5	-4.9	-4.9	-4.8
CHEMBL572044	-5.9	-5.8	-5.7	-5.7	-5.7	-5.7	-5.7	-5.5	-5.5	-5.5

CHEMBL589906	-5.9	-5.8	-5.7	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5
CHEMBL109	-5.8	-5.4	-5.4	-5.3	-5.3	-5.1	-5	-5	-5	-4.9
CHEMBL1096433	-5.8	-5.7	-5.5	-5.2	-5	-4.9	-4.8	-4.8	-4.7	-4.7
CHEMBL1099096	-5.8	-5.7	-5.7	-5.6	-5.5	-5.5	-5.4	-5.4	-5.4	-5.4
CHEMBL154517	-5.8	-5.7	-5.6	-5.6	-5.6	-5.6	-5.5	-5.5	-5.5	-5.5
CHEMBL1630114	-5.8	-5.7	-5.6	-5.6	-5.6	-5.5	-5.4	-5.4	-5.4	-5.3
CHEMBL1631918	-5.8	-5.4	-5.4	-5.1	-4.9	-4.9	-4.8	-4.7	-4.7	-4.7
CHEMBL1767034	-5.8	-5.7	-5.7	-5.6	-5.5	-5.5	-5.5	-5.5	-5.5	-5.4
CHEMBL1767043	-5.8	-5.7	-5.7	-5.7	-5.7	-5.6	-5.5	-5.5	-5.4	-5.3
CHEMBL178456	-5.8	-5.4	-5.3	-5.2	-5.1	-5	-5	-5	-4.9	-4.9
CHEMBL1798008	-5.8	-5.8	-5.7	-5.6	-5.5	-5.5	-5.4	-5.4	-5.3	-5.3
CHEMBL1800250	-5.8	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3	-5.3	-5.3	-5.2
CHEMBL1800378	-5.8	-5.8	-5.7	-5.7	-5.7	-5.5	-5.4	-5.4	-5.4	-5.4
CHEMBL1822050	-5.8	-5.6	-5.5	-5.5	-5.4	-5.4	-5.3	-5.3	-5.2	-5.2
CHEMBL2046612	-5.8	-5.6	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3
CHEMBL2047682	-5.8	-5.7	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5	-5.4	-5.4
CHEMBL2179615	-5.8	-5.8	-5.6	-5.4	-5.3	-5.1	-5	-4.8	-4.8	-4.7
CHEMBL2336043	-5.8	-5.8	-5.7	-5.7	-5.5	-5.5	-5.5	-5.4	-5.3	-5.2
CHEMBL2347010	-5.8	-5.8	-5.7	-5.6	-5.6	-5.5	-5.5	-5.4	-5.4	-5.3
CHEMBL242473	-5.8	-5.6	-5.5	-5.5	-5.5	-5.5	-5.3	-5.2	-5.2	-5.2
CHEMBL387924	-5.8	-5.3	-5.2	-5.1	-5.1	-5	-4.9	-4.9	-4.8	-4.8
CHEMBL393361	-5.8	-5.4	-5.4	-5.4	-5.3	-5.3	-5.1	-5	-5	-5
CHEMBL467792	-5.8	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3	-5	-5
CHEMBL475043	-5.8	-5.4	-5.4	-5.4	-5.3	-5.2	-5.1	-5.1	-5	-4.9
CHEMBL475862	-5.8	-5.6	-5.5	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3
CHEMBL482272	-5.8	-5.7	-5.6	-5.6	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3
CHEMBL485771	-5.8	-5.5	-5.3	-5.3	-5.2	-5.2	-5.2	-5	-5	-5
CHEMBL487347	-5.8	-5.8	-5.5	-5.4	-5.4	-5.4	-5.2	-5.2	-5.2	-5.1
CHEMBL493249	-5.8	-5.8	-5.8	-5.6	-5.6	-5.6	-5.3	-5.3	-5.2	-5.2

CHEMBL494124	-5.8	-5.7	-5.6	-5.6	-5.5	-5.5	-5.4	-5.4	-5.3	-5.3
CHEMBL509207	-5.8	-5.6	-5.6	-5.6	-5.5	-5.5	-5.5	-5.5	-5.4	-5.3
CHEMBL515295	-5.8	-5.8	-5.7	-5.6	-5.5	-5.4	-5.3	-5.2	-5.2	-5.2
CHEMBL517869	-5.8	-5.6	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3
CHEMBL1094094	-5.7	-5.5	-5.5	-5.3	-5.3	-5.3	-5.3	-5.2	-5.2	-5.1
CHEMBL1096093	-5.7	-5.4	-5.4	-5.2	-5.1	-5	-4.9	-4.9	-4.8	-4.7
CHEMBL141909	-5.7	-5.7	-5.5	-5.5	-5.3	-5.3	-5.1	-5.1	-5	-5
CHEMBL1767031	-5.7	-5.1	-5	-5	-4.9	-4.8	-4.7	-4.6	-4.6	-4.5
CHEMBL1767033	-5.7	-5.7	-5.4	-5.3	-5.2	-5	-5	-4.9	-4.9	-4.9
CHEMBL2046609	-5.7	-5.4	-5.3	-5.3	-5.3	-5.2	-5.2	-5.2	-5.1	-5.1
CHEMBL2046614	-5.7	-5.6	-5.5	-5.5	-5.4	-5.3	-5.2	-5.2	-5.2	-5.1
CHEMBL2046618	-5.7	-5.4	-5.2	-5.1	-5.1	-5	-5	-4.9	-4.9	-4.8
CHEMBL2179618	-5.7	-5.6	-5.5	-5.4	-5.3	-5.3	-5.2	-5.2	-5.1	-5
CHEMBL2333342	-5.7	-5.5	-5.4	-5.3	-5.2	-5.2	-5.2	-5.2	-5.2	-4.9
CHEMBL245548	-5.7	-5.6	-5.5	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4	-5.4
CHEMBL261272	-5.7	-5.5	-5.5	-5.3	-5.1	-5.1	-5.1	-5	-4.9	-4.7
CHEMBL271949	-5.7	-5.5	-5.4	-5.3	-5.2	-5.2	-5.1	-5.1	-5	-5
CHEMBL356769	-5.7	-5.6	-5.5	-5.4	-5.3	-5.3	-5.2	-5.1	-5	-5
CHEMBL403323	-5.7	-5.6	-5.5	-5.3	-5.3	-5.3	-5.2	-5.1	-5.1	-5
CHEMBL453953	-5.7	-5.6	-5.5	-5.4	-5.3	-5.3	-5.3	-5.3	-5.2	-5.2
CHEMBL455395	-5.7	-5.1	-4.9	-4.7	-4.7	-4.7	-4.6	-4.6	-4.5	-4.5
CHEMBL462210	-5.7	-5.6	-5.5	-5.4	-5.4	-5.3	-5.3	-5.2	-5.2	-5.2
CHEMBL471174	-5.7	-5.7	-5.6	-5.5	-5.5	-5.2	-5.2	-5.2	-5.2	-5.1
CHEMBL473836	-5.7	-5.3	-5.2	-5.2	-5.2	-5.1	-5.1	-5.1	-5.1	-5
CHEMBL481719	-5.7	-5.4	-5.2	-5.2	-5	-4.9	-4.9	-4.8	-4.7	-4.7
CHEMBL494526	-5.7	-5.5	-5.5	-5.4	-5.3	-5.3	-5.3	-5.3	-5.2	-5.1
CHEMBL497331	-5.7	-5.5	-5.4	-5.3	-5.3	-5.3	-5.3	-5.2	-5.2	-5.1
CHEMBL507114	-5.7	-5.7	-5.7	-5.6	-5.3	-5.3	-5.3	-5.3	-5.3	-5.3
CHEMBL507592	-5.7	-5.5	-5.2	-5.1	-5.1	-5.1	-4.9	-4.8	-4.7	-4.7

CHEMBL516600	-5.7	-5.7	-5.6	-5.6	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4
CHEMBL519943	-5.7	-5.7	-5.5	-5.4	-5.4	-5.4	-5.3	-5.2	-5.2	-5.1
CHEMBL561483	-5.7	-5.5	-5.5	-5.2	-5.1	-5	-5	-5	-4.9	-4.9
CHEMBL561604	-5.7	-5.4	-5.4	-5.2	-5.2	-5	-4.9	-4.8	-4.8	-4.7
CHEMBL566807	-5.7	-5.6	-5.6	-5.6	-5.5	-5.5	-5.2	-5.1	-5.1	-5.1
CHEMBL571505	-5.7	-5.7	-5.7	-5.6	-5.5	-5.3	-5.3	-5.1	-5	-5
CHEMBL589311	-5.7	-5.2	-4.9	-4.7	-4.6	-4.6	-4.5	-4.5	-4.5	-4.5
CHEMBL1094708	-5.6	-5.3	-5.3	-5	-5	-5	-4.9	-4.9	-4.9	-4.8
CHEMBL1095136	-5.6	-5.5	-5.5	-5.4	-5.3	-5.3	-5.2	-5.2	-5.1	-5.1
CHEMBL1095710	-5.6	-5.5	-5.4	-5.4	-5.4	-5.4	-5.3	-5.3	-5.3	-5.2
CHEMBL1096986	-5.6	-5.6	-5.4	-5.3	-5.2	-5	-4.9	-4.9	-4.9	-4.8
CHEMBL1630113	-5.6	-5.6	-5.4	-5.3	-5.3	-5.1	-5.1	-5.1	-5	-5
CHEMBL1631912	-5.6	-5.5	-5.5	-5.4	-5.3	-5.3	-5.3	-5.2	-5.2	-5.2
CHEMBL1631914	-5.6	-5.3	-4.9	-4.8	-4.8	-4.6	-4.5	-4.5	-4.5	-4.4
CHEMBL1798003	-5.6	-5.4	-5.4	-5.3	-5.2	-5.2	-5.1	-5	-5	-5
CHEMBL1800376	-5.6	-5.6	-5.3	-5.2	-5.1	-5.1	-5	-4.9	-4.8	-4.8
CHEMBL1801238	-5.6	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3	-5.1	-5
CHEMBL2018304	-5.6	-5.4	-5.2	-5	-4.4	-4.3	-4.3	-4.3	-4.1	-3.8
CHEMBL2018448	-5.6	-5.5	-5.4	-5.4	-5.2	-5.1	-5	-5	-4.9	-4.8
CHEMBL2047538	-5.6	-5	-5	-4.8	-4.6	-4.5	-4.4	-4.4	-4.3	-4.3
CHEMBL2047692	-5.6	-5.3	-5.3	-5.1	-5.1	-5.1	-5.1	-5.1	-5.1	-5
CHEMBL2047702	-5.6	-5.6	-5.5	-5.4	-5.4	-5.3	-5.3	-5.2	-5.2	-5.2
CHEMBL216641	-5.6	-5.5	-5.5	-5.5	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3
CHEMBL2337867	-5.6	-5	-5	-4.9	-4.9	-4.7	-4.7	-4.6	-4.5	-4.3
CHEMBL244199	-5.6	-5.6	-5.5	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3	-5.2
CHEMBL247653	-5.6	-5.4	-5.4	-5.3	-5.3	-5.2	-5.1	-4.9	-4.9	-4.9
CHEMBL264411	-5.6	-5.2	-4.8	-4.7	-4.7	-4.6	-4.6	-4.6	-4.6	-4.6
CHEMBL343717	-5.6	-5.4	-5.4	-5.4	-5.3	-5.3	-5.2	-5.2	-5.2	-5.2
CHEMBL439842	-5.6	-5.5	-5.4	-5.3	-5.2	-5.2	-5.1	-5.1	-5	-5

CHEMBL466032	-5.6	-5.6	-5.6	-5.5	-5.4	-5.4	-5.3	-5.3	-5.2	-5.2
CHEMBL468935	-5.6	-5.5	-5.4	-5.2	-5.2	-5.2	-5	-4.9	-4.8	-4.7
CHEMBL473826	-5.6	-5.5	-5.5	-5.4	-5.4	-5.4	-5.4	-5.4	-5.3	-5.3
CHEMBL474051	-5.6	-5.5	-5.4	-5.3	-5.3	-5.3	-5.2	-5.2	-5.1	-5
CHEMBL474208	-5.6	-5.4	-5.4	-5.3	-5.2	-5.1	-5.1	-5.1	-5.1	-5
CHEMBL475051	-5.6	-5.5	-5.4	-5.2	-5.2	-5.1	-5.1	-5.1	-5.1	-5
CHEMBL492317	-5.6	-5.6	-5.5	-5.5	-5.4	-5.3	-5.3	-5.2	-5.2	-5.1
CHEMBL494813	-5.6	-5.5	-5.3	-5.3	-5.3	-5.2	-5.1	-5	-5	-5
CHEMBL573900	-5.6	-5.6	-5.6	-5.4	-5.3	-5.3	-5.2	-5.2	-5.2	-5.2
CHEMBL585554	-5.6	-5.4	-5.4	-5.3	-5.2	-5.1	-5.1	-5.1	-5.1	-5.1
CHEMBL138293	-5.5	-5.3	-5.1	-5.1	-5	-5	-4.9	-4.8	-4.8	-4.7
CHEMBL1800249	-5.5	-5.2	-5.2	-5.1	-5.1	-5.1	-4.9	-4.9	-4.8	-4.8
CHEMBL1800383	-5.5	-5.3	-5.3	-5.3	-5.3	-5.2	-5.1	-5.1	-5.1	-5
CHEMBL1836143	-5.5	-5.4	-5.3	-5.1	-5.1	-4.7	-4.7	-4.7	-4.7	-4.6
CHEMBL2018305	-5.5	-5.4	-5.2	-5.1	-5	-4.8	-4.7	-4.7	-4.6	-4.6
CHEMBL2018451	-5.5	-5.4	-4.9	-4.8	-4.8	-4.7	-4.6	-4.4	-4.4	-4.4
CHEMBL2047679	-5.5	-5.4	-5.4	-5.3	-5.3	-5.3	-5.3	-5.2	-5.1	-5.1
CHEMBL2047694	-5.5	-5.1	-5	-5	-4.9	-4.9	-4.9	-4.8	-4.8	-4.7
CHEMBL2048751	-5.5	-4.9	-4.9	-4.9	-4.8	-4.7	-4.7	-4.6	-4.6	-4.6
CHEMBL221655	-5.5	-5.3	-5.3	-5.3	-5.2	-5.2	-5.1	-5.1	-5.1	-5
CHEMBL2333339	-5.5	-5.3	-5.2	-5.2	-5.1	-5	-4.7	-4.5	-4.5	-4.5
CHEMBL2333341	-5.5	-5	-4.9	-4.9	-4.7	-4.7	-4.6	-4.4	-4.4	-4.4
CHEMBL260080	-5.5	-5.4	-5.4	-5.4	-5.3	-5.3	-5.3	-5.2	-5.2	-5.1
CHEMBL389688	-5.5	-5.2	-5.2	-5.1	-4.8	-4.7	-4.7	-4.6	-4.6	-4.5
CHEMBL461141	-5.5	-5.3	-5.2	-5.2	-5.2	-5.1	-5.1	-5.1	-5.1	-5
CHEMBL475301	-5.5	-5.4	-5.1	-5	-4.9	-4.9	-4.9	-4.8	-4.7	-4.7
CHEMBL475714	-5.5	-5.5	-5.3	-5.3	-5.2	-5.2	-5.2	-5.1	-5.1	-5
CHEMBL484073	-5.5	-5.5	-5.2	-5.1	-5.1	-4.9	-4.9	-4.9	-4.9	-4.8
CHEMBL511212	-5.5	-5.3	-5.3	-5.1	-4.9	-4.8	-4.7	-4.6	-4.5	-4.5

CHEMBL521652	-5.5	-4.9	-4.9	-4.8	-4.8	-4.7	-4.7	-4.7	-4.7	-4.6
CHEMBL583130	-5.5	-5.5	-5.3	-5.3	-5.3	-5.2	-5.2	-5.2	-5.2	-5.1
CHEMBL1095075	-5.4	-5.4	-5.1	-5.1	-5	-5	-4.9	-4.9	-4.9	-4.8
CHEMBL1095449	-5.4	-5.3	-5.3	-5.2	-5.1	-5	-5	-4.9	-4.9	-4.7
CHEMBL1096022	-5.4	-5.4	-5.2	-5.2	-5.2	-5.1	-5	-5	-4.9	-4.9
CHEMBL146250	-5.4	-5.3	-5.3	-5.2	-5.2	-5.2	-5.2	-5.2	-5.1	-5
CHEMBL1800244	-5.4	-5.4	-5.4	-5.1	-5	-5	-5	-4.9	-4.9	-4.9
CHEMBL2018446	-5.4	-5.3	-5.3	-5.3	-5.2	-5.2	-5.2	-5.2	-5.1	-5
CHEMBL259517	-5.4	-5.3	-5.2	-5.2	-5.2	-5.2	-5.2	-5.1	-5.1	-5.1
CHEMBL400721	-5.4	-5	-4.9	-4.9	-4.8	-4.7	-4.7	-4.6	-4.6	-4.6
CHEMBL427776	-5.4	-5.1	-5.1	-4.8	-4.8	-4.8	-4.6	-4.5	-4.5	-4.4
CHEMBL447397	-5.4	-5.3	-5.2	-5.2	-5.2	-5	-5	-5	-5	-5
CHEMBL467998	-5.4	-5.3	-5.3	-5.1	-5.1	-5.1	-5	-5	-5	-4.9
CHEMBL473270	-5.4	-5.2	-5.2	-5	-5	-4.9	-4.9	-4.9	-4.7	-4.7
CHEMBL481718	-5.4	-5.2	-5.1	-5.1	-5	-5	-4.9	-4.9	-4.8	-4.7
CHEMBL496512	-5.4	-5.2	-5.1	-5	-4.9	-4.9	-4.9	-4.8	-4.7	-4.6
CHEMBL517384	-5.4	-5.4	-5.4	-5.2	-5.2	-5.2	-5.1	-5.1	-4.8	-4.7
CHEMBL564876	-5.4	-5.3	-5.3	-5.1	-5.1	-5.1	-5.1	-4.9	-4.9	-4.9
CHEMBL1097017	-5.3	-5.3	-5.3	-5.3	-5.3	-5.3	-5.2	-5.2	-5.2	-5.2
CHEMBL1800251	-5.3	-5.3	-5.2	-5.2	-5	-5	-5	-4.9	-4.9	-4.8
CHEMBL1914708	-5.3	-5.2	-5.2	-5.2	-5.2	-5.2	-5.1	-5.1	-5.1	-5.1
CHEMBL2018445	-5.3	-5.1	-5	-5	-5	-4.9	-4.9	-4.9	-4.8	-4.7
CHEMBL247218	-5.3	-5.3	-5.2	-5.1	-5.1	-5	-5	-5	-4.9	-4.9
CHEMBL253309	-5.3	-5.1	-5.1	-5.1	-4.9	-4.8	-4.7	-4.7	-4.7	-4.7
CHEMBL261587	-5.3	-5.1	-5	-4.9	-4.8	-4.8	-4.8	-4.8	-4.8	-4.7
CHEMBL482287	-5.3	-5.2	-4.9	-4.9	-4.9	-4.9	-4.8	-4.8	-4.7	-4.7
CHEMBL1096705	-5.2	-5.1	-5.1	-4.9	-4.8	-4.7	-4.6	-4.6	-4.6	-4.5
CHEMBL14227	-5.2	-5	-5	-5	-4.8	-4.8	-4.8	-4.8	-4.8	-4.7
CHEMBL1630115	-5.2	-5.1	-5	-5	-5	-5	-5	-4.9	-4.8	-4.6

CHEMBL1798002	-5.2	-5.2	-5.2	-5.1	-5.1	-5	-5	-5	-5	-4.9
CHEMBL1818136	-5.2	-5.1	-5	-5	-4.9	-4.9	-4.8	-4.7	-4.7	-4.6
CHEMBL2337872	-5.2	-5	-5	-5	-4.9	-4.8	-4.7	-4.7	-4.7	-4.6
CHEMBL440018	-5.2	-5.1	-5	-5	-5	-5	-5	-4.9	-4.8	-4.8
CHEMBL460088	-5.2	-5.1	-5.1	-5	-5	-5	-4.9	-4.9	-4.8	-4.7
CHEMBL480884	-5.2	-5.2	-5.1	-5	-5	-5	-4.9	-4.9	-4.9	-4.9
CHEMBL512517	-5.2	-5	-5	-4.9	-4.8	-4.8	-4.8	-4.5	-4.5	-4.4
CHEMBL515764	-5.2	-5.2	-5.1	-5	-4.9	-4.9	-4.8	-4.8	-4.8	-4.6
CHEMBL573899	-5.2	-5.2	-5.1	-5.1	-5.1	-5	-5	-4.9	-4.9	-4.8
CHEMBL1099094	-5.1	-5.1	-5.1	-5.1	-5.1	-4.9	-4.9	-4.8	-4.8	-4.7
CHEMBL140525	-5.1	-5.1	-5	-4.8	-4.8	-4.5	-4.5	-4.5	-4.5	-4.5
CHEMBL2047542	-5.1	-5.1	-5.1	-5	-5	-4.9	-4.8	-4.8	-4.8	-4.7
CHEMBL2047685	-5.1	-5.1	-5	-4.9	-4.9	-4.8	-4.8	-4.7	-4.6	-4.6
CHEMBL2177587	-5.1	-4.8	-4.4	-4.3	-4.3	-4.2	-4.2	-4	-3.9	-3.9
CHEMBL2178343	-5.1	-5	-4.9	-4.8	-4.8	-4.7	-4.7	-4.6	-4.6	-4.6
CHEMBL236902	-5.1	-5.1	-5.1	-5.1	-5	-5	-5	-5	-5	-4.9
CHEMBL238596	-5.1	-5.1	-4.9	-4.9	-4.9	-4.9	-4.8	-4.8	-4.8	-4.8
CHEMBL246199	-5.1	-5	-5	-5	-4.9	-4.7	-4.7	-4.7	-4.6	-4.6
CHEMBL468595	-5.1	-5	-5	-4.9	-4.8	-4.8	-4.7	-4.7	-4.7	-4.6
CHEMBL475618	-5.1	-5.1	-5	-5	-4.9	-4.9	-4.9	-4.9	-4.9	-4.9
CHEMBL494990	-5.1	-5.1	-5	-4.9	-4.9	-4.9	-4.8	-4.8	-4.7	-4.7
CHEMBL497760	-5.1	-5	-5	-4.9	-4.9	-4.8	-4.8	-4.8	-4.7	-4.7
CHEMBL518821	-5.1	-5.1	-4.5	-4.4	-4.4	-4.1	-4.1	-4.1	-4	-3.9
CHEMBL569306	-5.1	-5.1	-4.9	-4.8	-4.8	-4.8	-4.8	-4.8	-4.7	-4.7
CHEMBL1094793	-5	-4.9	-4.9	-4.9	-4.9	-4.8	-4.8	-4.8	-4.8	-4.7
CHEMBL1095120	-5	-5	-4.9	-4.9	-4.8	-4.7	-4.7	-4.7	-4.7	-4.6
CHEMBL1095972	-5	-4.9	-4.8	-4.7	-4.6	-4.6	-4.6	-4.5	-4.5	-4.5
CHEMBL1099095	-5	-4.8	-4.7	-4.7	-4.7	-4.6	-4.5	-4.5	-4.5	-4.5
CHEMBL1165082	-5	-5	-4.8	-4.5	-4.5	-4.5	-4.5	-4.5	-4.4	-4.4

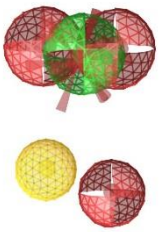
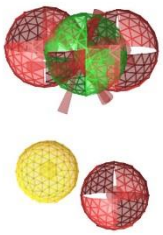
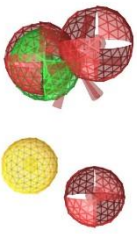
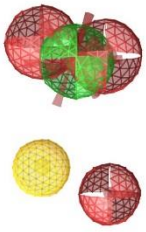
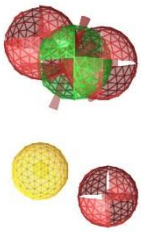
CHEMBL1214761	-5	-4.8	-4.7	-4.6	-4.6	-4.6	-4.5	-4.4	-4.2	-4.2
CHEMBL140000	-5	-4.8	-4.7	-4.6	-4.6	-4.6	-4.5	-4.5	-4.5	-4.5
CHEMBL152162	-5	-5	-5	-4.9	-4.6	-4.6	-4.6	-4.6	-4.6	-4.5
CHEMBL154574	-5	-4.8	-4.8	-4.7	-4.7	-4.7	-4.6	-4.6	-4.6	-4.6
CHEMBL1631913	-5	-4.8	-4.7	-4.7	-4.6	-4.5	-4.3	-4.2	-4.2	-4.1
CHEMBL1767041	-5	-4.6	-4.5	-4.5	-4.5	-4.4	-4.3	-4.1	-4.1	-4
CHEMBL1808672	-5	-4.9	-4.8	-4.6	-4.6	-4.5	-4.5	-4.5	-4.5	-4.5
CHEMBL2337870	-5	-5	-4.9	-4.8	-4.7	-4.7	-4.6	-4.6	-4.6	-4.5
CHEMBL466215	-5	-5	-5	-4.9	-4.9	-4.9	-4.9	-4.9	-4.8	-4.8
CHEMBL481726	-5	-5	-4.9	-4.9	-4.8	-4.8	-4.7	-4.7	-4.6	-4.6
CHEMBL493783	-5	-4.9	-4.8	-4.8	-4.6	-4.6	-4.6	-4.5	-4.5	-4.4
CHEMBL503	-5	-5	-4.9	-4.8	-4.8	-4.7	-4.6	-4.6	-4.5	-4.5
CHEMBL510856	-5	-4.8	-4.7	-4.7	-4.6	-4.6	-4.6	-4.5	-4.5	-4.5
CHEMBL1095718	-4.9	-4.9	-4.6	-4.5	-4.5	-4.5	-4.3	-4.3	-4.3	-4.3
CHEMBL180064	-4.9	-4.9	-4.8	-4.6	-4.5	-4.5	-4.4	-4.4	-4.4	-4.4
CHEMBL2046610	-4.9	-4.8	-4.8	-4.8	-4.7	-4.7	-4.6	-4.6	-4.6	-4.5
CHEMBL2047684	-4.9	-4.9	-4.7	-4.7	-4.6	-4.6	-4.6	-4.6	-4.5	-4.5
CHEMBL2047698	-4.9	-4.7	-4.7	-4.6	-4.6	-4.5	-4.5	-4.5	-4.4	-4.3
CHEMBL209453	-4.9	-4.9	-4.7	-4.7	-4.7	-4.6	-4.6	-4.6	-4.5	-4.5
CHEMBL271741	-4.9	-4.8	-4.7	-4.7	-4.6	-4.6	-4.6	-4.6	-4.4	-4.4
CHEMBL468527	-4.9	-4.9	-4.8	-4.7	-4.7	-4.6	-4.6	-4.6	-4.6	-4.4
CHEMBL494527	-4.9	-4.9	-4.8	-4.8	-4.7	-4.7	-4.6	-4.6	-4.5	-4.5
CHEMBL137875	-4.8	-4.7	-4.6	-4.6	-4.5	-4.5	-4.4	-4.4	-4.4	-4.4
CHEMBL1630118	-4.8	-4.7	-4.6	-4.4	-4.4	-4.4	-4.3	-4.3	-4.3	-4.2
CHEMBL1800245	-4.8	-4.7	-4.6	-4.6	-4.6	-4.5	-4.5	-4.5	-4.5	-4.5
CHEMBL461142	-4.8	-4.6	-4.6	-4.6	-4.5	-4.5	-4.4	-4.4	-4.3	-4.3
CHEMBL466459	-4.8	-4.8	-4.7	-4.7	-4.6	-4.6	-4.5	-4.5	-4.5	-4.5
CHEMBL479602	-4.8	-4.7	-4.7	-4.7	-4.6	-4.5	-4.5	-4.4	-4.3	-4.3
CHEMBL1630108	-4.7	-4.5	-4.5	-4.4	-4.3	-4	-4	-3.9	-3.9	-3.8

CHEMBL1800377	-4.7	-4.6	-4.5	-4.4	-4.3	-4.2	-4.2	-4.2	-4.1	-4
CHEMBL454672	-4.7	-4.6	-4.6	-4.6	-4.5	-4.5	-4.4	-4.4	-4.4	-4.3
CHEMBL494139	-4.7	-4.7	-4.7	-4.6	-4.6	-4.6	-4.6	-4.6	-4.6	-4.5
CHEMBL505259	-4.7	-4.5	-4.4	-4.3	-4.3	-4.3	-4.2	-4.2	-4.2	-4.2
CHEMBL1095451	-4.6	-4.5	-4.5	-4.4	-4.4	-4.4	-4.4	-4.3	-4.3	-4.3
CHEMBL427135	-4.6	-4.6	-4.6	-4.4	-4.3	-4.2	-4.1	-4.1	-4.1	-4
CHEMBL462370	-4.6	-4.4	-4.4	-4.4	-4.3	-4.3	-4.3	-4.3	-4.2	-4.2
CHEMBL479601	-4.6	-4.5	-4.4	-4.4	-4.4	-4.3	-4.3	-4.3	-4.3	-4.3
CHEMBL1767039	-4.5	-4.5	-4.4	-4.4	-4.3	-4.3	-4.2	-4.2	-4.2	-4.2
CHEMBL393360	-4.5	-4.5	-4.4	-4.4	-4.4	-4.4	-4.3	-4.3	-4.2	-4.2
CHEMBL405072	-4.5	-4.5	-4.4	-4.3	-4.3	-4.3	-4.2	-4.2	-4	-4
CHEMBL409860	-4.5	-4.4	-4.4	-4.4	-4.3	-4.3	-4.2	-4.2	-4.1	-4.1
CHEMBL487106	-4.5	-4.5	-4.4	-4.3	-4.1	-4.1	-4.1	-4.1	-4	-4
CHEMBL523033	-4.5	-4.4	-4.2	-4.1	-3.7	-3.6	-3.5	-3.4	-3.1	-3.1
CHEMBL1165292	-4.2	-3.7	-3.5	-3.5	-3.5	-3.4	-3.4	-3.2	-3.2	-3
CHEMBL492311	-4.2	-4.1	-3.7	-3.7	-3.7	-3.7	-3.6	-3.5	-3.2	-3.1
CHEMBL569122	-3.6	-3.6	-3.4	-3.3	-3.3	-3.3	-3.3	-3.3	-3.1	-3.1
CHEMBL506834	-3	-3	-3	-2.9	-2.9	-2.8	-2.7	-2.6	-2.6	-2.6
CHEMBL1095711	-1.2	-1.2	-1.1	-1	-1	-1	-0.9	-0.9	-0.9	-0.9
CHEMBL186311	-1.2	-1.2	-1.2	-1.1	-1	-1	-0.9	-0.9	-0.9	-0.8
CHEMBL2347008	-1.2	-1.2	-1.2	-1.2	-1.1	-1	-1	-1	-0.9	-0.9
CHEMBL259826	-1.2	-1.2	-1.1	-1.1	-1	-1	-1	-0.9	-0.9	-0.9
CHEMBL471043	-1.2	-1.2	-1.2	-1.1	-1	-1	-1	-1	-0.9	-0.9
CHEMBL574365	-1.2	-1.2	-1.2	-1.1	-1	-1	-1	-0.9	-0.9	-0.9

4.4. Pharmacophore Modelling

10 Models were generated with the pharmacophore scores ranging from 0.7363 to 0.7905. The pharmacophore fit scores of the training set and test set compounds were calculated. The best pharmacophore is the one which has highest pharmacophore score. The HDAC6_1 with

score of 0.7905 was identified as best model. The pharmacophore fit score of the training set molecules were in the range of 55.4400 to 64.9900. The table below shows the ten models along with pharmacophore scores and figures.

Pharmacophore Model	Pharmacophore Score	Pictorial Representaion
HDAC6_1	0.7905	
HDAC6_2	0.787	
HDAC6_3	0.7768	
HDAC6_4	0.7717	
HDAC6_5	0.7684	

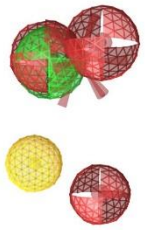
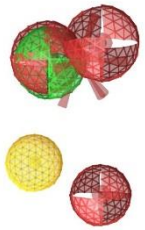
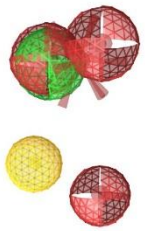
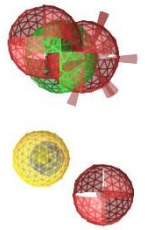
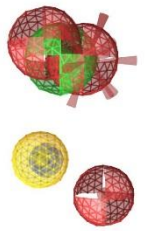
HDAC6_6	0.7674	
HDAC6_7	0.7663	
HDAC6_8	0.7653	
HDAC6_9	0.7371	
HDAC6_10	0.7363	

Figure 8. Pharmacophore models generated through Ligand-based Pharmacophore approach. The best model is represented at the top with the highest pharmacophre score.

4.4.1. Database Screening

The pharmacophore model HDAC6_1 was used to screen the drugbank database. The screening has led to identification of 106 hits which bear similar pharmacophoric features to the designed pharmacophore. The pharmacophore fit score of the compounds were in the range of 53.91 to 65.18 which are reported in the below table along with the 2D images of the hits.

Table 2: Hits identified by Pharmacophore model HDAC6_1 along with their pharmacophore fit score.

Compound Name	DrugBank_ID	Pharmacophore fit Score
273	DB00273	63.9355
unnamed molecule	DB00275	63.0052
710	DB00710	54.9228
xxxxxx	DB00795	55.2828
unnamed molecule	DB01014	54.9996
xxxxxx	DB01250	54.4694
unnamed molecule	DB01834	54.6478
unnamed molecule	DB01877	55.7397
IPO	DB01980	56.2886
unnamed molecule	DB01973	54.0872
GNR	DB02036	56.3878
CBP	DB02049	63.3385
GM6	DB02255	64.8937
unnamed molecule	DB02169	63.5983
MM3	DB02350	55.9091
unnamed molecule	DB02367	64.139
unnamed molecule	DB02546	65.177
unnamed molecule	DB02560	56.3023
ISA	DB02570	55.5354
unnamed molecule	DB02625	56.1518
LHY	DB02652	55.6382
unnamed molecule	DB02677	54.1287
FTT	DB02767	54.8347
unnamed molecule	DB02691	63.3972
DBD	DB02827	63.1456

unnamed molecule	DB02894	63.9548
NHB	DB02917	64.9878
unnamed molecule	DB02943	53.9076
unnamed molecule	DB03390	54.7957
LVA	DB03785	63.2229
BAT	DB03880	54.5914
unnamed molecule	DB04150	54.123
BBH	DB04140	63.7412
SPI	DB04232	64.5632
INF	DB04316	55.5788
TSN	DB04297	64.8024
BB2	DB04310	64.6912
BB1	DB04368	56.275
4TR	DB04600	63.7067
4TZ	DB04601	64.0293
CA2	DB04656	64.0197
114	DB06693	62.855
28	DB06830	55.2849
99	DB06837	64.5643
1C2	DB06887	63.972
294	DB06945	56.0343
252	DB06931	55.0314
2NI	DB06971	57.0963
2UN	DB06989	64.2485
37A	DB07026	63.7
347	DB07013	63.5403
4NH	DB07121	63.6123
4HD	DB07111	55.1889
541	DB07145	63.5793

4UN	DB07127	64.0977
7MR	DB07246	55.8185
915	DB07290	64.8206
AGE	DB07350	64.0483
B28	DB07409	54.3209
B08	DB07404	54.3492
B29	DB07410	54.4791
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CTF	DB07596	55.7044
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GB4	DB07818	56.5254
GB5	DB07819	56.187
FBD	DB07754	54.3048
GVR	DB07861	56.5265
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HPX	DB07914	63.5385
HOC	DB07907	55.6448
HXD	DB07930	54.9674
HTA	DB07926	64.2885
IH6	DB07964	56.5736
J54	DB08007	55.0421
JT5	DB08029	55.4295
JT6	DB08030	56.8622
KEL	DB08040	64.4558

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MP2	DB08199	54.5152
NGH	DB08271	55.7503
NVC	DB08310	64.1814
PLH	DB08403	64.2109
PO1	DB08416	55.7042
RO4	DB08482	64.7132
RP4	DB08485	63.9443
RS1	DB08490	63.5953
RRS	DB08489	63.8256
RS2	DB08491	56.8171
S17	DB08505	64.737
SB7	DB08523	56.4279
SB9	DB08525	56.45
SB8	DB08524	64.8359
SK2	DB08549	63.1838
SRB	DB08565	55.2985
SRD	DB08566	54.828
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V35	DB08692	56.1467
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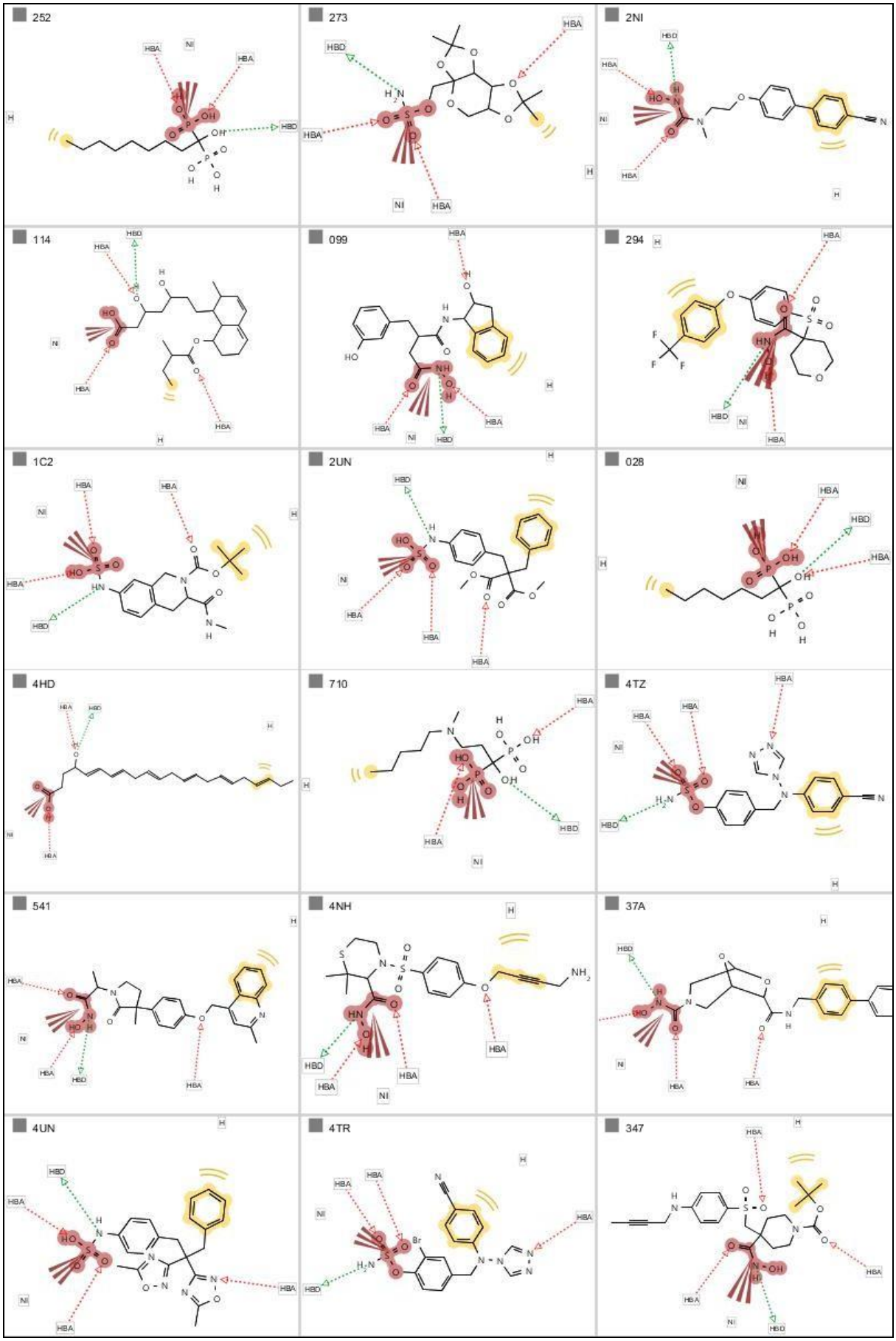
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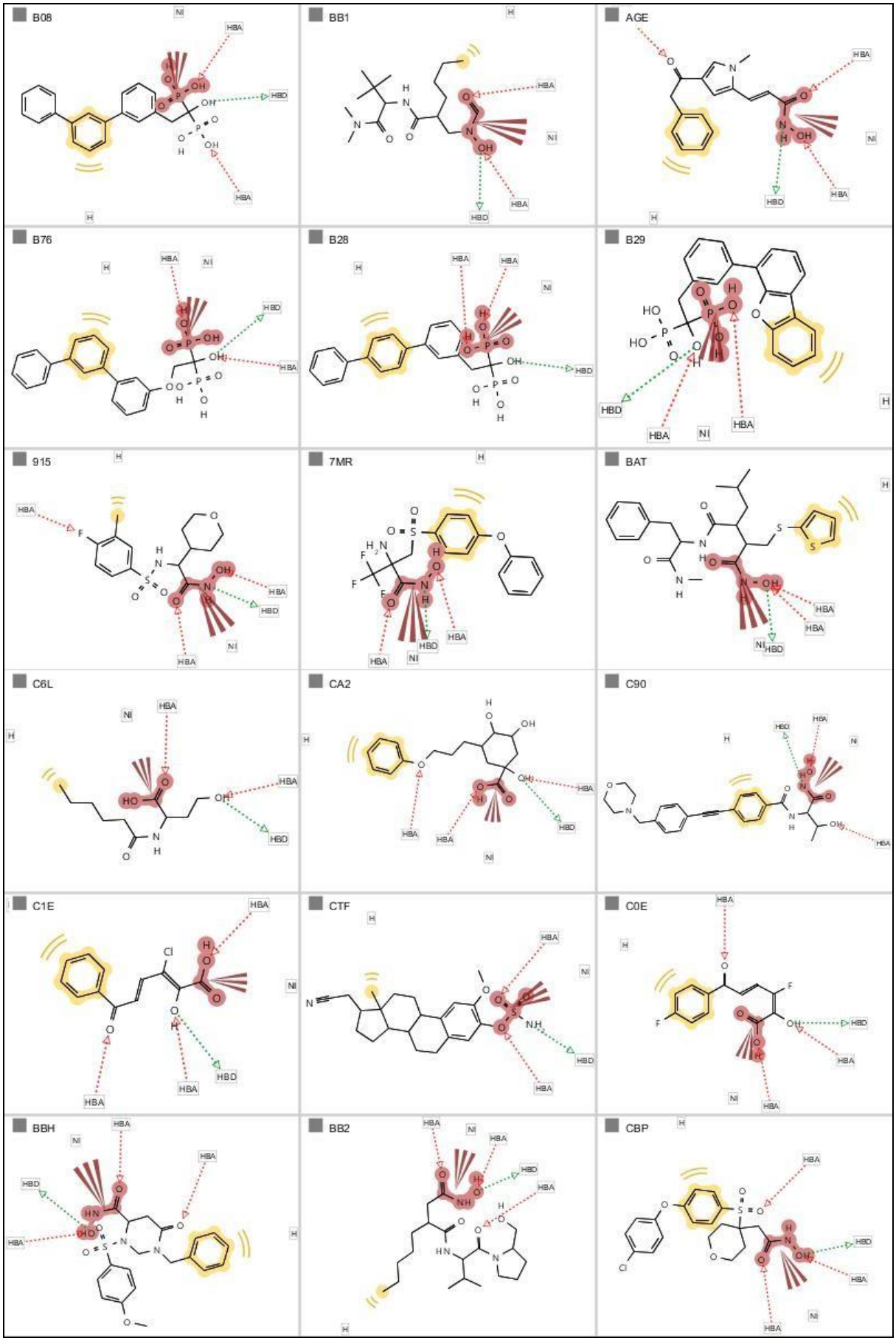
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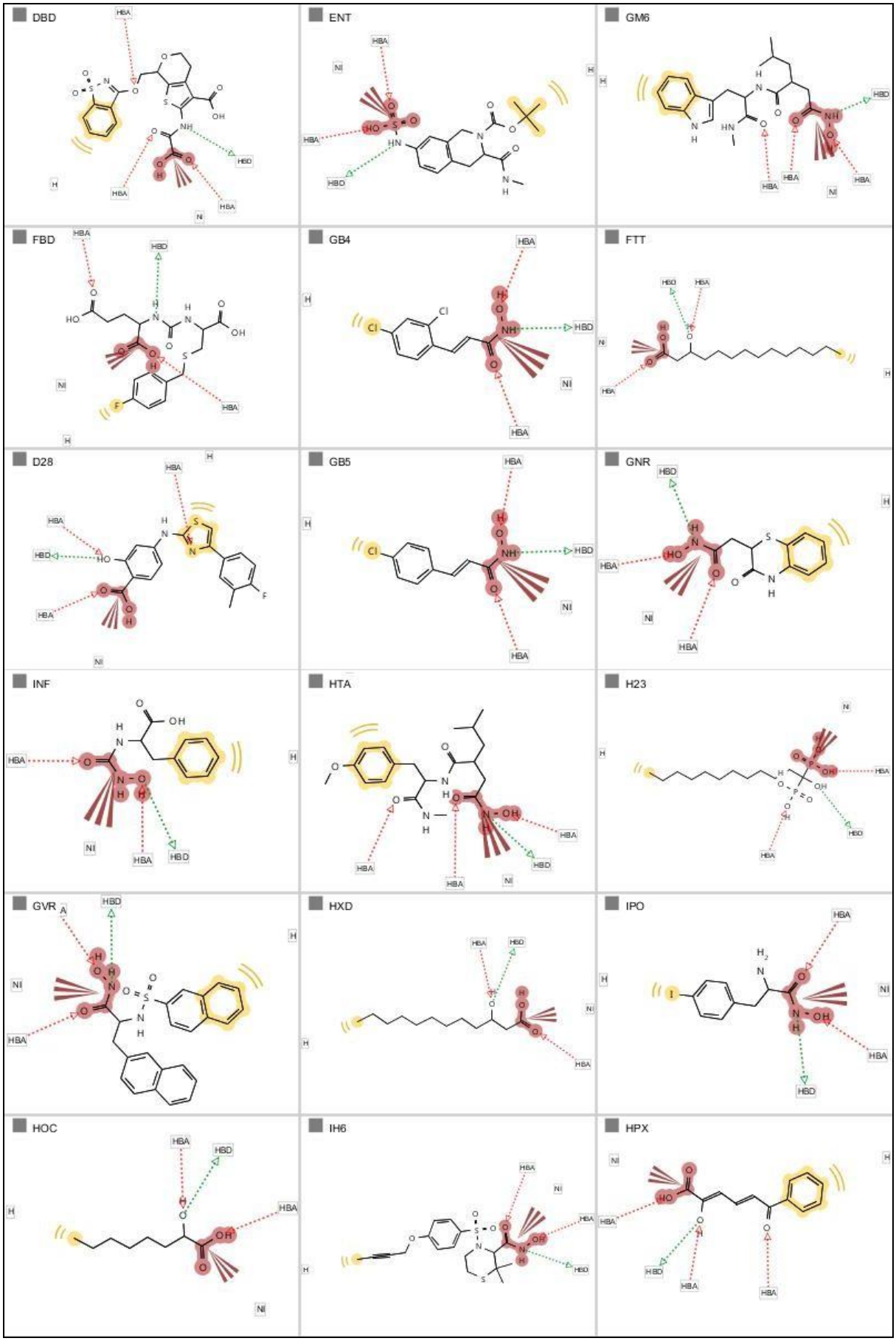
BB2
CBP

III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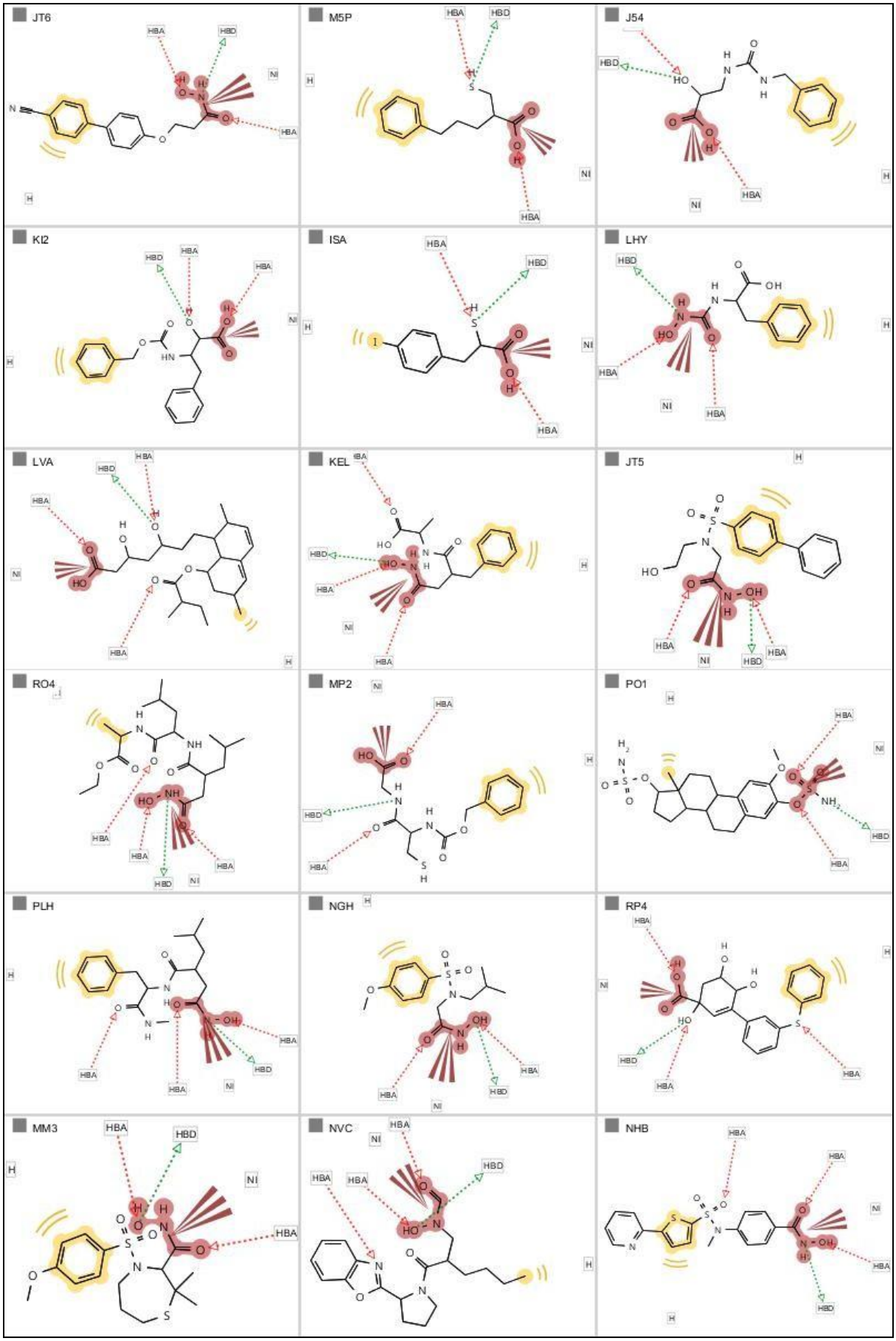
HPX

IV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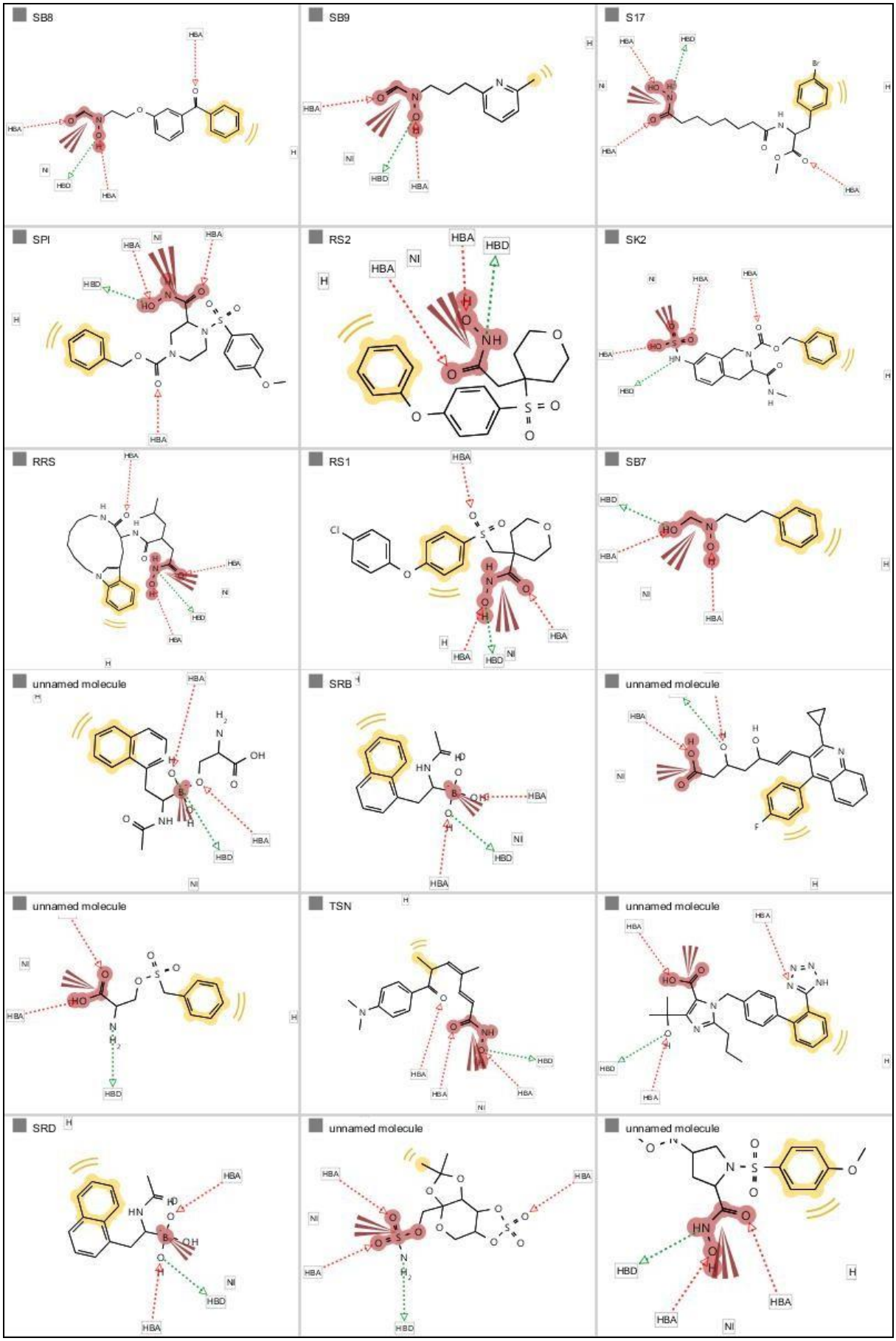
NHB

V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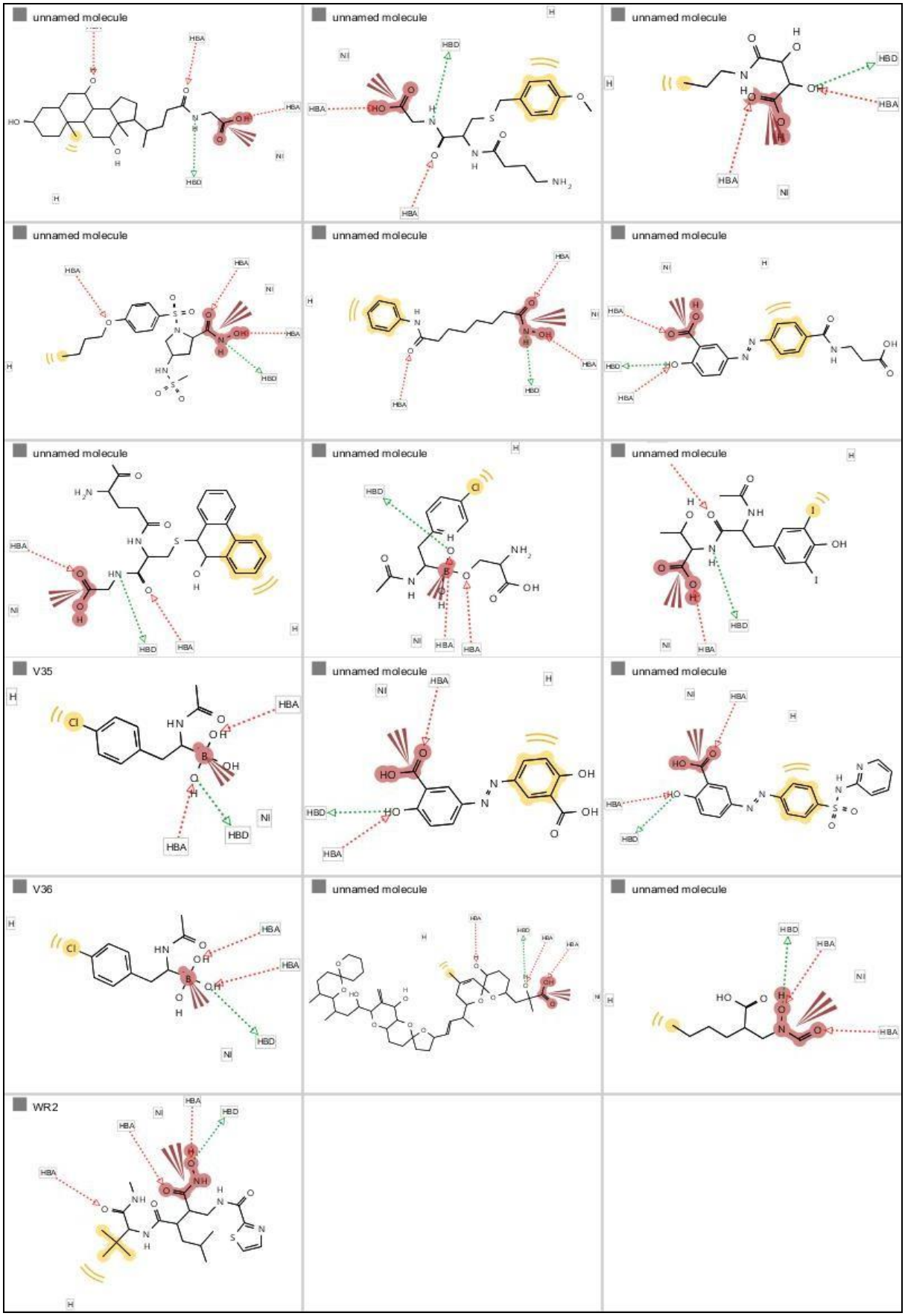
VI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V36
unnamed molecule
unnamed molecule
WR2

Figure 9. Images I – VI show the hits identified from the Drugbank by Pharmacophore Model.

4.5. Quantitative Structure Activity Relationship

4.5.1. Model Generation

McQSAR generated 5 models after 100 generations with input as 128 training set molecules. The models is represented by a equation which signifies the relation between the activity and structure of the molecules given. The Q^2 and R^2 values of the model were found to be 0.706566 and 0.726806 respectively. The equation representing the model is given below which was evolved over a number of generations through Genetic Algorithm.

IC50=plus(gauss(-534.14,1.02e+008,-83.7321,SHBint3),min(neg(plus(min(neg(min(neg(gauss(8.03342,4.10571,-0.359046,SHBint3)),qspline(1.86615,MDEC-12))),qspline(1.68416,MDEC-12)),gauss(1.94631,-10.7843,-0.428094,SHBint3))),plus(gauss(-53.0825,73.3457,-15.135,SHBint3),neg(plus(plus(min(neg(min(neg(plus(neg(neg(min(neg(plus(neg(plus(neg(neg(min(plus(neg(gauss(7.95504e+006,3.89645e+009,1.20794e+006,SHBint3)),gauss(7.03843,2.2964,0.205736,SHBint3)),qspline(1.86615,MDEC-12)))),gauss(7.97635,4.3048,0.432446,SHBint3))),min(neg(plus(neg(neg(min(neg(neg(min(neg(plus(neg(gauss(7.60386e+006,2.40802e+009,1.12006e+006,SHBint3)),gauss(-287377,-2.21213e+007,46154.3,SHBint3))),qspline(1.57048,MDEC-12)))),qspline(1.20426,MDEC-12)))),gauss(7.06853,-2.1651,-1.47862,SHBint3))),qspline(2.15509,MDEC-12)))),plus(neg(gauss(8.01102e+006,1.40084e+009,1.20234e+006,SHBint3)),gauss(6.83827,0.39254,1.95102,SHBint3))))),gauss(0.917709,4.60439,-11.3851,SHBint3))),qspline(3.66314,MDEC-12))),qspline(-1.92571,MDEC-

12)),neg(plus(gauss(14.6928,-3.17036,-0.316201,SHBint3),gauss(8.24637,3.60928,-0.313038,SHBint3)))),neg(neg(gauss(4.06945,1.2315,-0.497654,SHBint3)))))))

In the above equation max, min, plus and mul are binary operators representing maximum, minimum, addition and multiplication respectively, whereas exp, neg, log, sqrt, gauss, spline and qspline are unary operators representing exponential, negation, logarithm, squareroot, gaussian function, knot and knot to power of 2 respectively.

The descriptors that are used in the above equation are

SHBint3 - Sum of E-State descriptors of strength for potential Hydrogen Bonds of path length 3

MDEC-12 - Molecular distance edge between all primary and secondary carbons.

4.5.2. Prediction of Activity

IC50 values for 106 compounds identified as hits from DrugBank by pharmacophore model was predicted. The IC50 values were in the range of 0.923136 nM to 8473.64 Nm. The table below presents the Drugbank hits along with their predicted IC50 and molecular weights.

Table 3: IC50 values predicted by QSAR model generated by McQSAR

S.No	DRUGBANK_ID	MOLECULAR_WEIGHT	PREDICTED_IC50 (nM)
1	DB01980	306.1	0.923135814
2	DB08040	294.303	0.92436842
3	DB07516	252.65	0.925463937
4	DB07914	218.205	0.930439202
5	DB08482	401.498	0.932110714

6	DB02827	466.442	0.934988997
7	DB04656	310.342	0.935356352
8	DB08485	358.408	0.935603634
9	DB08199	312.342	0.936417454
10	DB08041	329.347	0.938307959
11	DB07536	437.488	0.939817007
12	DB07754	402.395	0.941229651
13	DB04150	576.122	0.945530408
14	DB08007	238.24	0.951642874
15	DB02652	224.213	0.962345678
16	DB04316	224.213	0.962345678
17	DB02677	361.177	0.965097076
18	DB02560	345.564	0.965837359
19	DB01834	501.552	0.967256373
20	DB07510	254.186	0.968741489
21	DB07410	448.3	0.980597022
22	DB07404	434.316	0.980755856
23	DB07409	434.316	0.981379722
24	DB07873	346.294	0.985108848
25	DB00710	319.229	0.986485509
26	DB06931	304.214	0.986880687
27	DB03390	191.182	0.988267105
28	DB06830	276.161	0.98847368
29	DB07426	450.315	0.989274171
30	DB07246	404.361	0.991569934
31	DB01973	259.279	1.293930649
32	DB07907	160.211	1.368626674
33	DB02943	383.463	1.504042125
34	DB08491	391.438	1.88357102

35	DB02049	425.883	2.555912606
36	DB08693	258.486	4.373982086
37	DB08692	258.486	4.373982086
38	DB06945	445.41	5.03133228
39	DB02570	308.136	5.883137516
40	DB02169	805.003	6.33041235
41	DB04297	302.368	7.959027403
42	DB07964	398.497	9.704027084
43	DB02350	374.476	11.00246511
44	DB02546	264.32	11.91434029
45	DB06837	370.399	14.91969689
46	DB08489	456.578	20.62718673
47	DB07026	383.398	20.73862697
48	DB08523	181.232	21.59384601
49	DB02036	238.263	25.9352238
50	DB07121	413.512	26.30449691
51	DB04310	385.498	26.65937723
52	DB08565	274.1	28.59433494
53	DB08566	274.1	28.59433494
54	DB03880	477.64	29.0255194
55	DB02367	435.516	34.92207173
56	DB07145	433.5	36.11602958
57	DB08733	455.572	37.65390304
58	DB08271	316.373	38.42111817
59	DB08490	425.883	42.47662477
60	DB07532	217.262	51.40081439
61	DB02917	389.449	55.60578805
62	DB02691	465.623	58.53558998
63	DB04368	329.435	65.72945026

64	DB06971	311.335	66.98537608
65	DB01877	345.371	67.23106641
66	DB08029	350.39	67.89378175
67	DB07350	284.31	85.78275699
68	DB08030	282.294	86.73612184
69	DB07818	232.063	98.14315159
70	DB07819	197.618	109.7539097
71	DB04232	449.478	114.5829502
72	DB04140	419.452	114.6700495
73	DB07861	420.481	140.6662792
74	DB08310	359.42	340.3063085
75	DB02255	388.461	347.0084097
76	DB00795	398.393	624.3383323
77	DB01014	357.318	624.3383323
78	DB01250	302.239	624.3383323
79	DB02894	361.346	624.3383323
80	DB04600	449.282	624.3383323
81	DB04601	370.386	624.3383323
82	DB07616	344.36	624.3383323
83	DB08161	224.319	624.3383323
84	DB08860	421.461	624.3383323
85	DB00273	339.362	652.5743508
86	DB08549	419.452	685.0306447
87	DB07290	346.374	776.4616313
88	DB07013	465.563	1020.234487
89	DB02767	244.37	1307.073471
90	DB03785	422.555	1307.073471
91	DB06693	408.528	1307.073471
92	DB06989	407.438	1307.073471

93	DB07111	344.488	1307.073471
94	DB07127	455.487	1307.073471
95	DB07596	404.523	1307.073471
96	DB07930	216.317	1307.073471
97	DB08416	460.565	1307.073471
98	DB08403	349.425	1315.164265
99	DB06887	385.435	1432.385777
100	DB07719	385.435	1432.385777
101	DB00275	446.502	1475.230898
102	DB07926	379.451	2307.0659
103	DB08524	285.295	3773.722837
104	DB08505	429.306	5855.715927
105	DB08525	194.23	8299.272031
106	DB02625	189.209	8473.639821

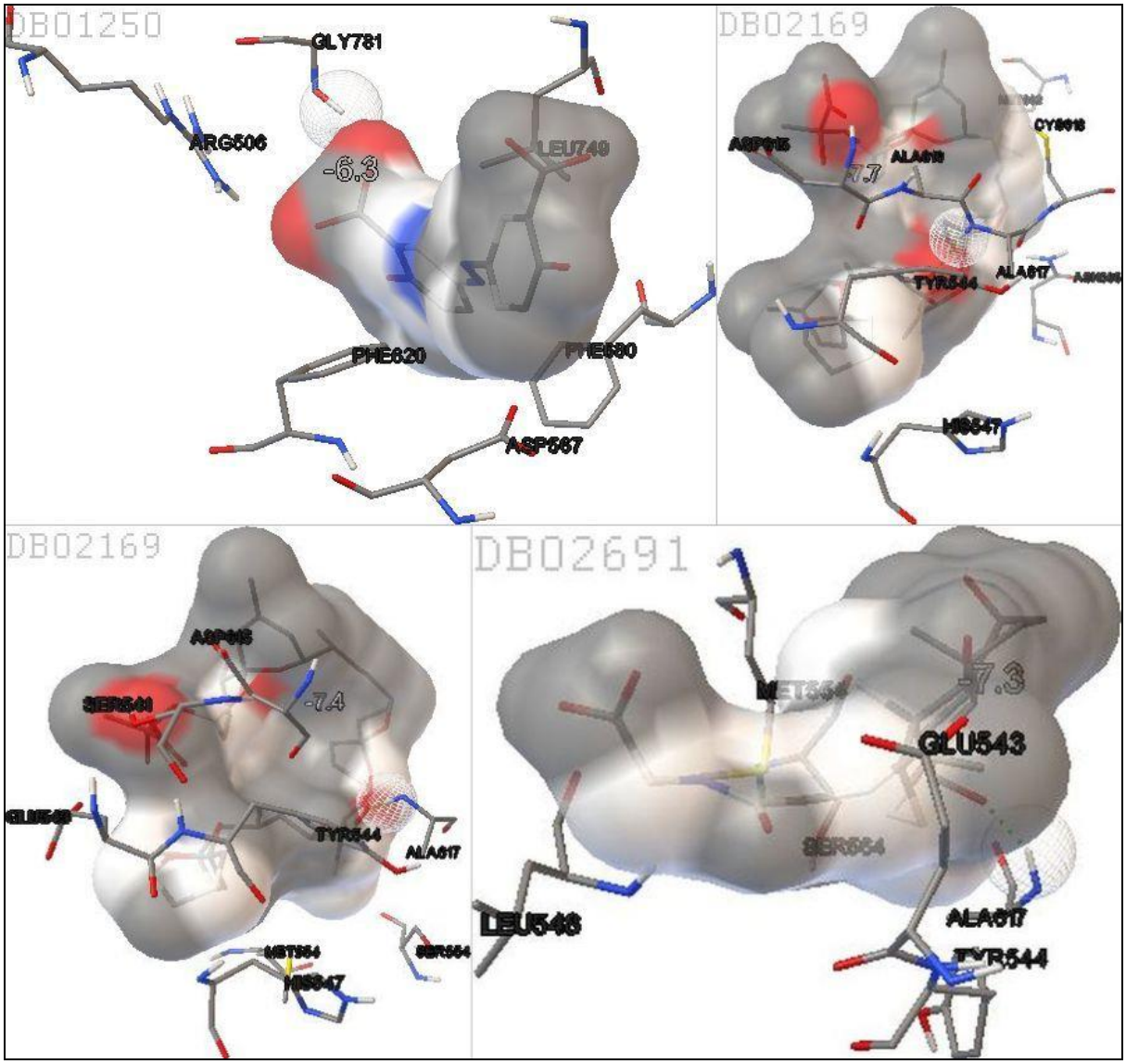
4.6. Estimation of Free Binding Energy

The binding energy for 58 compounds were estimated by Autodock vina. 8 molecules possessing binding energy less than -7 were selected for interaction studies. The top three binding poses were analysed for the presence of hydrogen bonds. It was found that most of the hydrogen bonding is with the residue ALA 617, present in the binding pocket. The table below summarizes the results of docking.

Table 4. Binding energies of top Drugbank hits along with their hydrogen bonding residues.

DrugBank_ID	Binding Energies of top three conformation		
DB01250	-7.1	-7.1	-6.3
			GLY781
DB02169	-7.7	-7.6	-7.4
	ALA617		ALA617

DB02691	-7.3	-7.1	-6.8
	ALA617		GLY619
DB06837	-7.2	-6.8	-6.5
		ALA617	
DB06945	-7	-6.8	-6.8
		TYR 570, ALA617	
DB07026	-7.4	-7.4	-7.2
			TYR 570,ALA617
DB07145	-7.3	-7.3	-7.1
		LEU548, ALA617	TYR 570,ALA617
DB08549	-7.2	-6.6	-6.6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GLY781
ARG506
-6.3
LEU749
PHE620
PHE630
ASP667
DB02169
ASP615
ALA616
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CYS618
TYR544
ALA617
HIS547
DB02169
ASP615
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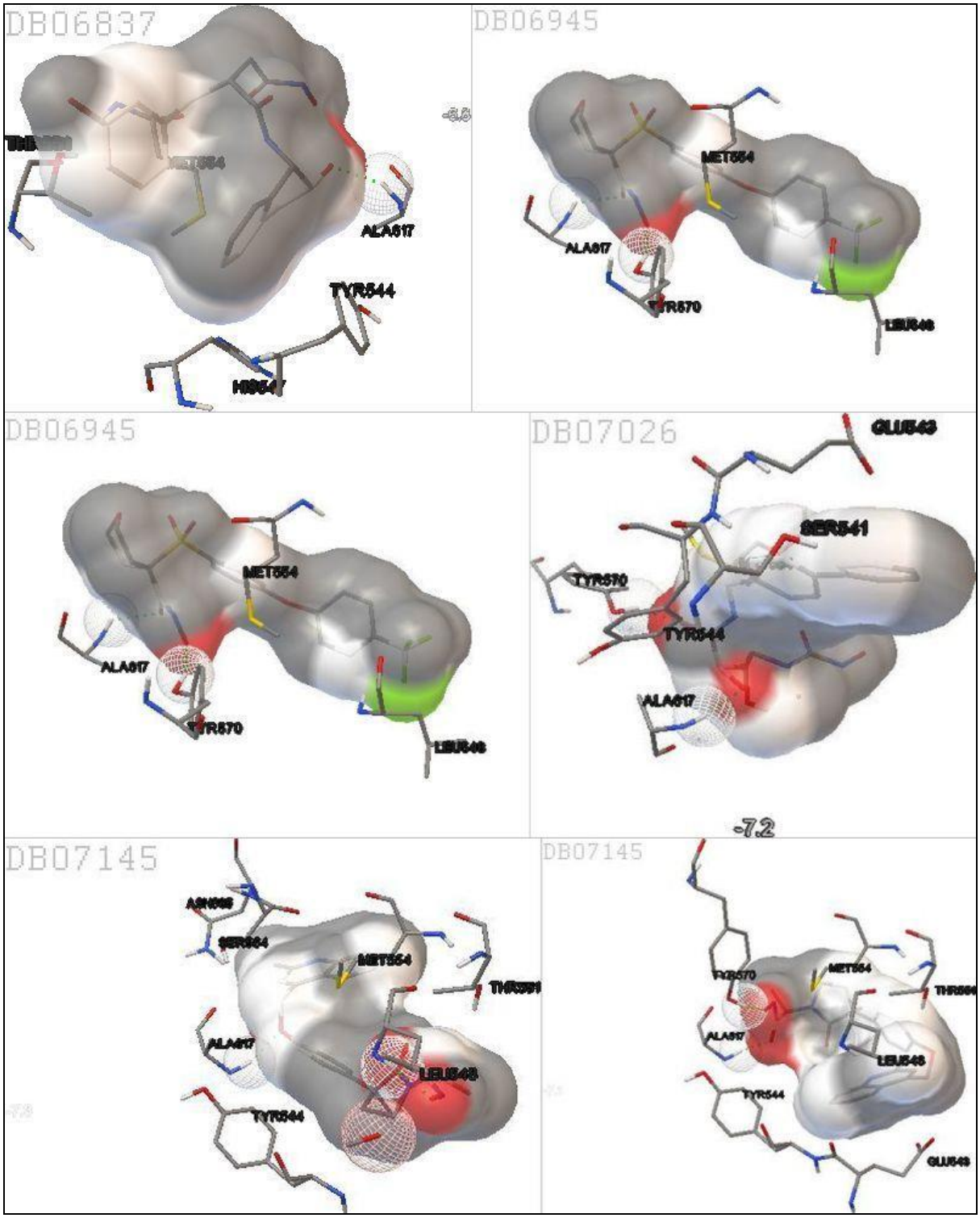

Figure 10. Docked conformations showing interactions between protein and ligand with hydrogen bonding represented as a wireframe.

CHAPTER 5
CONCLUSION

5. Conclusion

The need for specific inhibitors of Histone deacetylase 6 without affecting the function of other crucial HDACs is addressed in the present study. A rigorous screening procedure involving search for compounds in drugbank by the built pharmacophore, prediction of activity by QSAR and docking studies has led to the identification of 8 compounds that could prove to be a potential inhibitors of HDAC6. The work also emphasized on the importance of the structure of protein in the process of drug discovery. The need for structure was addressed by building a modelled protein using multiple templates. Most of the compounds discovered so far are hydroxamic acid based small molecules. The present study is able to look beyond them at compounds such as Benzenoids, Glycosides, Steriod derivatives, Ethers, Pyrrolidines and Carboxylic acids. A highly efficient pharmacophore developed in this study could be further used to screen compounds from various other databases such as NCI, ZINC, etc. A further docking study against its closest isoforms may help in establishing its specificity against HDAC6. The suggested compounds could be tested for their in-vitro capability for inhibition and their toxic effects against normal cells.

CHAPTER 6
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